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Alachlor Special Review Position Document 1

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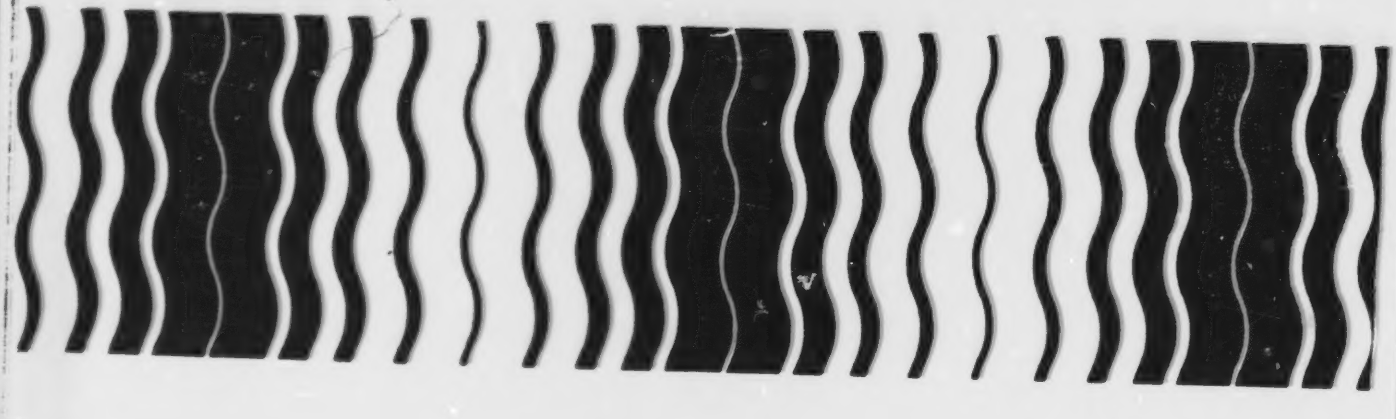
Special Review Position Document 1



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EXECUTIVE SUMMARY

This Position Document (PD) 1 presents the basis for the initiation of a Special Review of all pesticide products containing the active ingredient, alachlor. Laboratory studies in rats and mice have demonstrated the potential for alachlor to produce tumors in mammals. The Agency has determined that the weight of evidence demonstrates that alachlor is oncogenic to laboratory animals and, in the absence of data on humans, it is prudent to treat alachlor as a probable human carcinogen. Further, certain uses of alachlor are associated with significant exposures, therefore, the Agency has determined that certain uses of alachlor may result in unreasonable adverse effects to man.

The major pesticidal uses of alachlor are the preemergent application to field corn, soybeans and peanuts, which comprise about 99% of the chemical's use. The remaining uses, also involving preemergent application, are on sweet corn, popcorn, cotton, dry beans, grain sorghum, green peas, lima beans (green), sunflowers and ornamentals.

The Agency has determined that use of products containing alachlor poses a risk to human health through significant exposure to a substantial number of workers involved in application of pesticides. Moreover, the general public is exposed to alachlor in the diet from residues in treated crops and in drinking water in certain areas.

A preliminary analysis of the benefits associated with each registered use demonstrates that viable, effective alternatives are available and in use.

The following regulatory options will be considered by the Agency in reaching the proposed regulatory decision:

(1) Continuation of registration without changes.

(2) Continuation of registration with modification to terms and conditions of registration.

(3) Cancellation of registration.

Certain labeling restrictions have been required in the alachlor Registration Standard in order to address the risks from alachlor use during the period necessary to complete the administrative process initiated by this Position Document (See Chapter I.B.2). These measures are intended to address

ALACHLOR

POSITION DOCUMENT 1

OFFICE OF PESTICIDE PROGRAMS
UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
DECEMBER 31, 1984

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16. ABSTRACT

The Office of Pesticide Programs, U.S. Environmental Protection Agency (U.S. EPA) has prepared a Alachlor Position Document. This document presents the bases for the initiation of a Special Review of all pesticide products containing the active ingredient alachlor. The alachlor document is an extensive review of the following topics:

- Regulatory and legal background of alachlor
- Qualitative risk assessment, including metabolic and pharmacokinetic properties, short-term tests, oncogenicity and human studies.
- Exposure assessment
- Dietary risks and applicator risks, and
- Benefits summary

17. KEY WORDS AND DOCUMENT ANALYSIS

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EPA Form 2220-1 (Rev. 4-77) PREVIOUS EDITION IS OBSOLETE risks to applicators and the general public during and after use of the pesticide:

(1) Use of protective clothing;

(2) Tumor hazard warning statement;

(3) Water contamination warning statement;

(4) Prohibition of aerial application;

(5) Prohibition of use on potatoes; and

(6) Handling instructions to reduce applicator exposure.

A special information and training program available to all applicators is being required in the alachlor Registration Standard. Also, data to more fully assess ground water contamination and runoff contamination of surface water are being required on an accelerated schedule.

It is emphasized that this Special Review, which presumes against registration and continued registration of alachlor under the present terms and conditions, is not a notice of intent to cancel the registration of the pesticide, and may or may not lead to cancellation.

This Position Document invites all registrants, applicants and interested parties to comment and submit evidence in rebuttal of the presumptions listed in Chapter II of this document.

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I. Introduction

A. General Background and Organization

The Federal Insecticide, Fungicide and Rodenticide Act, as amended (FIFRA) [7 U.S.C. 136 et seq.], requires the Environmental Protection Agency (EPA) to review the risks and benefits of the uses of pesticides suspected of causing unreasonable adverse effects to human health or the environment.

In November, 1984, EPA issued another document, "Guidance for the Registration of Pesticide Products Containing Alachlor as an Active Ingredient" (Registration Standard). As part of developing that assessment, the Agency stated its determination that alachlor (2-chloro-2',6'-diethyl-N-(methoxymethyl)-acetanilide, CAS number 15972-60-8, meets one of the risk criteria used to determine whether it causes unreasonable adverse effects [40 CFR 162.11(a)(3)(ii)(A)]. In response to that determination, a Special Review is being initiated on alachlor. This review was prompted by studies showing that alachlor caused oncogenic effects in test animals. This Position Document (PD 1) reviews the Agency's assessment of the risks and benefits of the uses of alachlor, particularly the uses on peanuts, field corn and soybeans, and requests registrants and other interested persons to submit rebuttals and other information on the presumption and to submit any other data on the risks and benefits of alachlor.

This document contains four chapters. This introductory section, Chapter I, provides background information on alachlor and the pesticide regulatory process through which the chemical will pass, resulting in an Agency regulatory decision. Chapter II evaluates the potential human health risks of alachlor, and briefly describes the laboratory evidence of toxicity, available exposure data and the Agency's assessment of risk. Part III summarizes the economic benefits of alachlor and the assumptions and limits of the assessment of benefits. Chapter IV solicits additional information with respect to possible adverse effects from exposure to alachlor and describes the procedures by which interested parties may submit such information.

B. Legal Background

1. The Statute

The Federal Insecticide, Fungicide and Rodenticide Act, as amended (FIFRA) [7 U.S.C. 136 et seq.] requires the Environmental Protection Agency (EPA) to regulate all pesticide products through review of the risks and benefits of the uses of these products. The Administrator must determine that the use of a pesticide will not result in "unreasonable adverse effects on the environment," defined in Section 2(bb) of FIFRA as "any unreasonable risk to man or the environment, taking into account the economic, social and environmental costs and benefits of the use of any pesticide." In other words, any decision on pesticide registration must take into account both risks and benefits from the pesticide's use.

Section 6(b) of FIFRA authorizes the Administrator to issue a notice of intent to cancel the registration of a pesticide or to change its classification if it appears that the pesticide or its labeling "does not comply with the provisions of [FIFRA] or, when used in accordance with widespread and commonly recognized practice, generally causes unreasonable adverse effects on the environment".

The Administrator may also cancel the registration of a pesticide if its labeling does not comply with the misbranding provisions of FIFRA which require the labeling to contain language "adequate to protect health and the environment" [FIFRA Section 2(q)].

2. The Registration Standard Process

Under FIFRA Section 3(g), Congress has directed EPA to determine whether it can re-register all previously registered products so as to bring their registrations and their data bases into compliance with current requirements. To effect this, the Agency has developed new review procedures. Under those procedures, EPA publishes documents called "Registration Standards," each of which discusses a particular pesticide active ingredient. Each Registration Standard summarizes all the data (in its files) used in the Agency's development of a comprehensive regulatory position on the conditions and requirements for registration of all existing and future products which contain the active ingredient. These conditions and requirements, which must be met to obtain or retain full registration or reregistration under Section 3(c)(5) of FIFRA, include the submission of needed scientific data which the Agency does not now have, compliance with standards of toxicity, composition, labeling, packaging and satisfaction of the data compensation provisions of FIFRA Section 3(c)(1)(D).

The Registration Standard review process also includes a comparison of information about potential adverse effects of the specific uses of the pesticide with risk criteria listed in 40 CFR 162.11(c), and thereby assists in determining whether a product should be a candidate for the Special Review Process.

3. The Special Review Process

The Special Review Process provides a mechanism through which the Agency gathers risk and benefit information about pesticides which appear to pose risks of adverse effects to human health or the environment which may be unreasonable. Through issuance of various position documents (PDs), the

Agency invites pesticide registrants, USDA, FDA, user groups, environmental groups and other interested persons to participate in the Agency's review of suspect pesticides.

The Special Review regulations in 40 CFR 162.11(c)(5) prescribe regulatory criteria for the Agency's preliminary assessment of a pesticide's health and environmental effects and provide that a Rebuttable Presumption Against Registration (RPAR or Special Review) shall arise if the Agency determines that any of the risk criteria have been met.

Benefits evidence, submitted to and/or gathered by the Agency, must be evaluated and considered in light of the risk information. If the Agency determines that the risks appear to outweigh the benefits, the Agency can initiate action under FIFRA Section 6(b)(1) to cancel the registration for all or for specific uses, or to cancel the registration unless the terms and conditions of the registration or use are modified to adequately reduce the risks of continued use. FIFRA Section 6(b)(2) proceedings are appropriate where a pesticide use appears to pose unreasonable adverse effects, and the Agency seeks to obtain additional information on risk or benefits during an administrative hearing in order to make a decision on the ultimate fate of the pesticide's uses.

C. Regulatory History of Alachlor

1. Uses and Registration

Alachlor is produced in the United States by Monsanto Chemical Co. It has been registered since 1969 as a selective herbicide for control of many preemergent broadleaf weeds and grasses. Registered uses include selective weed control in cultivated agricultural land and woody ornamentals.

Alachlor is registered for use against a number of weed and grass species. Among the target species are barnyardgrass, crabgrass, foxtails, goosegrass, signalgrass, witchgrass, fall and Texas panicum, nightshade, carpetweed, pigweed, purslane and sandbur.

Alachlor is usually applied as a broadcast surface treatment by ground or air equipment using 15 or more gallons of water per acre. It may also be applied as a band treatment. The most commonly used formulations are the 43.5 and 45.1% emulsifiable concentrates (EC) and the 10 and 15% granular (G) products. A microencapsulated (ME) formulation was registered in 1983 for use on dry beans, lima beans, peas, potatoes, and soybeans. The alachlor EC formulations are generally applied as tank mixes with other herbicides. Alachlor also is sold in formulations mixed with either atrazine or glyphosate. Application rates vary from 1.5 to 8 pounds active ingredient per acre depending upon target species and use site.

According to EPA records, Monsanto is the only company holding Federal registrations for nine alachlor products. There are also nine intrastate registrations for alachlor which are marketed pursuant to 40 CFR 162.17.

2. Tolerances

Tolerances were established in 40 CFR 180.249 for alachlor and its metabolites (calculated as alachlor) resulting from the use of the herbicide in or on raw agricultural commodities. Tolerances are maximum permissible residue levels established pursuant to the Federal Food, Drug and Cosmetic Act. These tolerances are presented in Table 1.

There are also several pending petitions for alachlor tolerances in which additional tolerances have been requested for sugarcane at .2 parts per million (ppm), sugarcane forage and fodder at .2 ppm, cabbage at .3 ppm, sweet corn at .2 ppm, sweet corn forage and fodder at .5 ppm, and soybean hay at 1.0 ppm. Petitions are also pending which request an increase in the peanut tolerance from 0.05 ppm to .1 ppm and an increase in the potato tolerance from 0.1 ppm to 1.0 ppm. During the Special Review, the Agency will not be inclined to grant these pending tolerance petitions.

Table 1. Alachlor Tolerances

Commodity	Tolerance	Citation and Form	
Beans, dry	0.1 ppm	(40 CFR 180.249 Alachlor and its metabolites calculated as alachlor)	
Beans, forage	0.2 ppm		
Beans, lima (green)	0.1 ppm		
Cattle, fat	0.02 ppm		
Cattle, meat-by-products	"	"	"
Cattle, meat	"	"	"
Corn, fodder	0.2 ppm	"	"
Corn, forage	"		
Corn, fresh, including kernels and corn with husks removed	0.05 ppm	"	"
Corn, grain	0.2 ppm	"	"
Cotton, forage	"	"	"
Cottonseed	0.05 ppm	"	"
Eggs	0.02 ppm	"	"
Goats, fat	"	"	"
Goats, meat-by-products	"	"	"
Goats, meat	"	"	"
Hogs, fat	"	"	"
Hogs, meat-by-products	"	"	"
Hogs, meat	"	"	"
Horses, fat	"	"	"
Horses, meat	"	"	"
Milk	"	"	"
Peanuts	0.05 ppm	"	"
Peanuts, forage	3.0 ppm	"	"
Peanut, hay	"	"	"
Peanut, hulls	1.5 ppm	"	"
Peas, forage	0.2 ppm	"	"
Peas, hay	"	"	"
Peas, pods removed	0.1 ppm	"	"
Potatoes	"	"	"
Poultry, fat	0.02 ppm	"	"
Poultry, meat-by-products	"	"	"
Poultry, meat	"	"	"
Sheep, fat	0.02 ppm	"	"
Sheep, meat-by-products	"	"	"
Sheep, meat	"	"	"
Sorghum, fodder	1.0 ppm	"	"
Sorghum, forage	"	"	"
Sorghum, grain (milo)	0.1 ppm	"	"
Soybeans	0.2 ppm	"	"
Soybean, forage	0.75 ppm	"	"
Soybean, hay	0.2 ppm	"	"
Sunflower seed	0.25 ppm	"	"

3. Registration Standard and Special Review

The preparation of the Registration Standard for alachlor was initiated in 1982. The Registration Standard for alachlor has been developed and was published in November, 1984. During the analysis, the Agency reviewed information about the potential adverse effects, most specifically oncogenicity, associated with uses of alachlor that met the risk criterion listed in 40 CFR 162.11 (c). Based on that information the Special Review is being initiated for the pesticide.

Certain labeling restrictions are being required in the alachlor Registration Standard in order to address the risks from alachlor use during the period necessary to complete the Special Review process. The labeling restrictions include:

(1) Use of protective clothing;

(2) Tumor hazard warning statement;

(3) Water contamination warning statement;

(4) Prohibition of aerial application;

(5) Prohibition of use on potatoes; and

(6) Handling instructions to reduce applicator exposure.

These measures are intended to address risks to applicators and the general public during and after use of the pesticide. These labeling restrictions are discussed further in Chapter II.E.

The Agency is requiring additional data on an accelerated basis on the leaching and mobility of alachlor to examine the potential of alachlor to contaminate ground water. In addition, a monitoring study to evaluate the manner and extent of contamination of ground and surface water is being required.

A special information and training program available to all users of alachlor is also being required in the Registration Standard.

II. Risk Assessment

In reviewing the available data on alachlor during the Registration Standard process, the Agency determined that the risk criterion for oncogenicity (40 CFR 162.11(C)(5)) was met. This section consists of the oncogenicity risk assessment, incorporating many of the procedures and principles espoused by the Agency (NAS, 1983; OSTP, 1984; EPA, 1984).

The risk assessment process consists of four steps. In the first step, Hazard Identification, all relevant information is presented and a qualitative weight-of-the-evidence judgment is reached on the likelihood that the pesticide is a human carcinogen. In the second step, Dose-Response Assessment, experimental data are used in conjunction with certain assumptions and a mathematical model to extrapolate the likely upper bound of human cancer risk to the low dose range. The third step is Exposure Assessment in which human exposures via various routes and sources are estimated. Finally, in the fourth step, Risk Characterization, the results of the Exposure and Dose-Response Assessments are coupled to project the plausible upper bound of the cancer risk under different conditions of exposures. This step also includes a summary of the strength of the qualitative evidence, plus a treatment of the uncertainties in the final assessment.

A. Hazard Identification (Qualitative Risk Assessment)

1. Physical-Chemical Properties and Exposure Pathways

Alachlor is the common name for 2-chloro-2',6'-diethyl-N-(methoxymethyl)acetanilide, CAS number 15972-60-8, a pre-emergent herbicide. Other names for this pesticide include 2-chloro-N-(2,6-diethylphenyl)-N-(methoxymethyl)acetamide, CP 50144 and Lasso.

Alachlor has an empirical formula of $C_{14}H_{20}NO_2Cl$, a molecular weight of 269.77. Table 2 lists chemical and physical properties of alachlor.

Alachlor is registered for use as a pre-emergence herbicide on corn, soybeans and other crops. Corn and soybeans account for 98% of total alachlor usage. This use pattern and the environmental behavior of alachlor suggest that the principle pathways of human exposure are by direct contact during application and ingestion of foodstuffs and drinking water which contain alachlor residues.

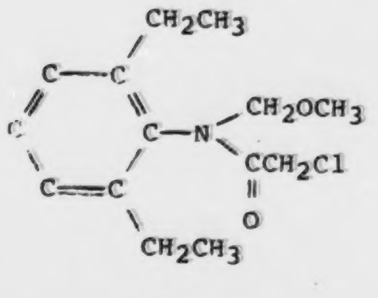
Table 2. Physical and Chemical Properties of Alachlor[1]

Melting Point	--	40-41°C
Specific Gravity	--	1.133(25/15.6°C)
Solubility	--	Soluble in ether, acetone, benzene, alcohol(unspecified) and ethyl acetate; slightly soluble in hexane; solubility in water - 240 ppm
Octanol/Water Partition Coefficient	--	434
Stability	--	Stable (first detectable heat evolution at 105°C)
Appearance at room temp.	--	White, crystalline solid at 23°C.

[1] Monsanto, 1973, 1979.

2. Structure-Activity Relationships

Alachlor is a substituted acetanilide. The Agency has concluded that at least one other chemical in this class is oncogenic in laboratory animals. Metolachlor (2-chloro-2'-ethyl-6'-methylphenyl-N(2-methoxy-1-methylethyl) acetanilide) has produced tumors in the rat liver (Ciba-Geigy, 1979). Other structurally-related chemicals have either not been adequately tested or the review of testing has not yet been completed by the Agency.



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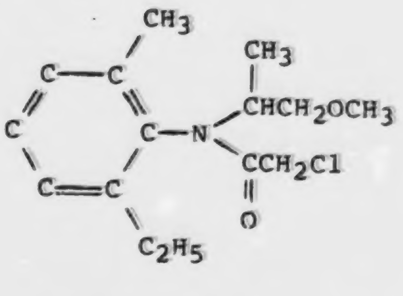

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3. Metabolic and Pharmacokinetic Properties

A gavage metabolism study in the rat (Monsanto, 1983a) indicated that alachlor is rapidly metabolized and eliminated as conjugates of mercapturic acid, glucuronic acid and sulfate in urine and feces (37.6 to 45.0% in urine and 47.7 to 51.1% in feces of males; 42.5 to 53.2% in urine and 37.0 to 49.3% in feces of females). Appproximately 89% of the dosages were eliminated during the 10-day study, with most of the elimination occurring within the first 48 hours (half life of .2 to 10.6 hours), followed by a slower phase (half life of 5 to 16 days). Elimination as CO_2 was minimal.

Radioactivity from the administered dose was found in the blood and in the spleen, liver, kidney and heart which may be a reflection of the amount of blood in those organs. In addition, a relatively high level of radioactivity was also found in the eyes, brain, stomach and ovaries. These data assume added significance in light of the treatment-related lesions observed in the 2-year rodent feeding studies discussed below.

A dermal absorption study (Monsanto, 1981a) in Rhesus monkeys indicated that approximately 50% of dermally applied alachlor EC formulation was absorbed within 24 hours. Additional *in vitro* dermal absorption studies were performed with human skin which suggest that the dermal absorption of the microencapsulated product may be approximately 12% (Monsanto, 1981b). However, due to difficulties associated with these studies, e.g. low recovery of the test material and metabolites, the usefulness of these data are limited. Additional data on dermal absorption are being required through the Registration Standard. No information is available on absorption by the inhalation route of exposure, but, as noted below, inhalation exposure of applicators appears to be insignificant compared to dermal exposure.

4. Non-Oncogenic Toxicological Effects

Alachlor exhibits relatively low acute toxicity by the oral (rat LD_{50}=.93 g/kg), dermal (rabbit LD_{50}=13.3 g/kg), or inhalation (rabbit LC_{50}>5.1 ml/l) routes of exposure (Monsanto, 1978a and 1981c). Although technical alachlor is a skin sensitizer and causes ocular lesions upon chronic exposure, the technical product has only slight skin and eye irritation potential after an acute exposure (Monsanto, 1978b and 1984a).

A two year rat feeding study in the Long-Evans strain showed alachlor to be toxic at all doses tested (14.0, 42.0 and 126.0 mg/kg/day) (Monsanto, 1982). The principal toxic effects observed were hepatotoxicity and an ocular lesion, referred to as the uveal degeneration syndrome (UDS). UDS is characterized in its mildest form by free floating iridial and choroidal pigment in the ocular chamber and pigment deposition on the cornea and lens. In its most severe form, the syndrome is characterized by bilateral degeneration of the iris and diminution of the size of the ocular globe with secondary total cataract formation.

A follow-up two-year feeding study in the same strain of rat was conducted at 0.5, 2.5 and 15.0 mg/kg/day (Stout, 1983a). There was a small increase at the high dose of animals exhibiting the initial stage of UDS, specifically molting of retinal pigmentation. The 2.5 mg/kg/day was judged to be the NOEL for UDS.

The Agency has subsequently received a study in Long-Evans rats run concurrently with the previously discussed study utilizing a higher dose of alachlor, 126 mg/kg/day, administered for less than a lifetime (Stout, 1983b). This study indicated that UDS, once established, is an irreversible condition. UDS has not been observed in the other toxicology studies that have been conducted to date.

In a six-month dog feeding study, alachlor was tested at 5.0, 25.0, 50.0 and 75.0 mg/kg/day and showed dose related hepatotoxicity at all doses (Ahmed, 1981). Increased absolute and relative liver weights were observed at all dose levels for males and at dose levels of 25 mg/kg/day and above for females. Liver fatty degeneration and biliary hyperplasia occurred in both sexes at dose levels of 25 mg/kg/day and greater.

In a three generation rat reproduction study, alachlor was tested at 3.0, 10.0 and 30.0 mg/kg/day and showed a reproduction NOEL at 10.0 mg/kg/day and reproduction lowest-observed-effect-level at 30.0 mg/kg/day, with indications of renal toxicity observed in F2 adult males and F3 pups (Schroeder, 1981). The renal toxicity consisted of kidney discoloration, chronic nephritis and increased relative and absolute kidney weights.

In a teratology study in the rat (Rodwell, 1980), alachlor was administered by gavage at dose levels of 50, 150 and 400 mg/kg/day. A maternal and fetotoxic NOEL was established at 150 mg/kg/day in this study with no teratogenic potential indicated at the highest dose tested, 400 mg/kg/day.

An additional rabbit teratology study was recently submitted but was considered inadequate to assess the teratogenic potential of alachlor due to the use of an inappropriate vehicle, only minimal evidence of maternal toxicity, a high incidence of preimplantation loss in the high dose, inadequate historical data, lack of individual fetal data for body weights and variations as well as other problems (Schardein, 1983).

5. Short Term Tests

The available mutagenicity testing data on alachlor are limited. A rec-assay was conducted at 6 concentrations (20 to 20,000 ug/plate) in *B. subtilis* strains M45 and H17 and showed no evidence of test compound-induced inhibition. The reverse mutation assay conducted at 6 concentrations (10 to 15,000 ug/plate) in *E. coli* strain WP2 *hcr* and *S. typhimurium* strains TA1538, TA1537, TA1535, TA98 and TA100, with and without S9 metabolic activation, was also negative (Shirasu, 1980).

A recently submitted in vitro/in vivo hepatocyte DNA repair study in rats indicated that alachlor is weakly genotoxic at 1000 mg/kg in the Fischer 344 strain of rat (Mirsalis, 1984). A recently submitted in vivo bone marrow cytogenetics study (Farrow, 1984) was determined to be negative for mutagenic potential but is considered to be scientifically unacceptable due to the lack of demonstration of the appropriateness of the dose levels used. As outlined in the Registration Standard, additional genotoxicity testing information is being required.

6. Oncogenicity

Alachlor feeding studies have demonstrated oncogenic effects which include lung tumors in mice and stomach, thyroid, and nasal turbinate tumors in rats. The results of these studies are described below.

Female mice of the CD-1 strain fed technical grade alachlor in the diet for 18 months at dosage rates of 26, 78 and 260 mg/kg/day developed a statistically significant increase ($p<0.05$) in lung bronchioalveolar tumors at the highest dose tested (Daly, 1981a). The increase of lung tumors in male mice was not significant. Numerical increases were observed in the incidence of liver and uterine tumors in the high dose group but these increases were not statistically significant. The technical material in this study was stabilized with epichlorohydrin (0.5%) for the first eleven months and with another intentionally added inert for the remainder of the study. This change in material tested came about because the registrant removed epichlorohydrin from technical alachlor, replacing it with a different stabilizer.

Two chronic feeding studies were conducted in the Long Evans strain of rat with alachlor. In the first study, the technical material was stabilized with epichlorohydrin during the first year of the study (Daly, 1981b) and fed to 50 animals/sex at dose levels of 14, 42, and 126 mg/kg/day. During the second year of this study, alachlor stabilized with another intentionally added inert was the test material.

Dose-related responses were observed for tumors of the nasal turbinate of both sexes for the mid and high doses. Also, statistically significant increases were observed in the incidence of malignant stomach tumors (described by the authors as neoplasms pluripotent in ability to form a mixed carcinomasarcoma-type tumor) in the high dose of both sexes ($p<0.001$). In addition, thyroid follicular tumors (adenomas plus carcinomas) appeared to increase in both sexes at the high-dosage level with the increase being significant ($p<0.001$) in males. The incidences of the nasal turbinate, stomach and thyroid tumors as well as other tumors, i.e. liver and brain, considered of potential biological significance is shown in Table 3. Table 3 also presents the histological diagnoses of the tumors of interest.

Table 3. Tumor Incidence in Rats

Dosage	(Stout 1983b) #ML-80-224				(Stout 1983a) #ML-80-186								(Daly 1981b) #BD-77-421							
mg/kg/day	12[illegible]				0		.5		2.5		15		0		14		42		126	
No. of tissues examined and incidence of animals with tumors	GI*		GIII*																	
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Nasal turbinate tumors	61	25	17	46	44	42	47	42	44	47	45	48	46	49	46	47	41	45	42	48
°Adenoma	42	11	10	19	0	0	0	0	0	1	15	14	0	0	0	0	10	4	23	10
°Adenocarcinoma	7	2	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0
Stomach	68	31	20	49	50	50	50	50	50	50	49	48	49	50	50	50	50	50	50	50
°Malignant tumors	3	19	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	1	17	23
-Mixed carcinomasarcoma	2	6	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	11	17
-Undifferentiated sarcoma	-	5	-	1	-	-	-	-	1	-	-	-	-	-	-	-	-	-	-	-
-Undifferentiated carcinoma	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
-Adenocarcinoma	-	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	2	1
-Leiomyosarcoma	-	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	1
-Anaplastic sarcoma	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
-Osteosarcoma	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	3	4
Thyroid	70	31	20	49	49	49	50	49	49	49	49	47	48	49	50	44	49	46	50	49
°C-cell adenoma	4	3	1	2	5	2	3	2	7	4	6	3	4	2	5	3	2	4	7	3
carcinoma	0	0	0	1	0	0	0	0	1	0	0	0	1	0	1	0	0	1	0	0
°Follicular adenoma	8	4	1	3	2	1	4	1	3	0	4	2	1	0	0	0	1	2	11	2
carcinoma	10	0	1	1	1	3	0	1	1	1	2	1	0	0	0	0	0	0	2	2
Brain	70	31	20	49	50	50	50	50	50	50	49	49	50	50	50	50	50	50	50	50
°Neuroepithelioma	1	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
°Ependymoma	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	2	1
Liver	70	31	20	49	50	50	50	50	50	50	50	49	50	50	50	50	50	50	50	50
°Hepatoma	3	1	0	0	1	0	0	1	0	0	0	0	1	0	0	0	2	1	1	3
°Nodular hyperplasia	0	1	0	1	0	0	0	0	0	0	0	1	0	2	0	1	1	2	4	1
°Carcinoma	2	2	0	1	2	0	1	1	2	0	0	2	0	0	0	0	0	0	0	0

*GI: animals maintained on treated diets for 2-year; GIII: animals maintained on treated diets for only 5 to 6 months.

In the second two-year feeding study (Stout, 1983a), throughout which an inert different from epichlorohydrin was used as a stabilizer in the test material, three treatment groups of 50 male and 50 female Long-Evans rats received 0.5, 2.5, and 15 mg/kg/day. Data from an additional study which ran concurrently with the previously discussed study have recently been submitted (Stout, 1983b). This additional study (Stout, 1983b) used a fourth treatment group, 126 mg/kg/day, that was exposed to the new technical material (with the new stabilizer in place of epichlorohydrin). The design of this study was different from the previous study (Stout, 1983b) because it used a variety of dosing regimens and had the primary purpose of investigating the nature and reversibly of the ocular lesions (UDS). The animals in this additional dose level were subdivided into three groups. One group was sacrificed and examined after approximately 8 months of treatment, one was treated for five to five and one half months and then put on control diet for the remainder of the two year period and the third group was treated for the entire two year period. The second group was selected from among the larger group primarily on the basis of appearance of early ocular effects rather than random assignment. The biased selection process inherent in the design of this study limits its usefulness for the quantitative assessment of oncogenic potential. However, the results are useful in qualitative assessment of the weight-of-the-evidence for the oncogenicity of the new technical product not stabilized with epichlorohydrin. This study indicates that the tumor response observed in the earlier study (Daly, 1981b) cannot be explained by the presence of epichlorohydrin in the test material and suggests that partial lifetime exposure (approximately one-fourth of the lifespan of the animals) can result in a similar tumor incidence as a lifetime exposure.

The nasal epithelial adenoma response was statistically significant in both sexes of both chronic rat studies ($p<0.001$). The incidence of this neoplasm in the second chronic rat study is presented in Table 3. In addition to the tumors presented in the table, it should be noted that there was a submucosal gland adenocarcinoma observed in a mid-dose male in the second study (Stout, 1983a). For risk assessment purposes, this submucosal gland adenocarcinoma was not combined with the adenomas and adenocarcinomas of the nasal turbinate because it was sufficiently different from other nasal tumors observed to be considered as not treatment related.

An increase was also noted in the incidence of thyroid follicular cell adenomas or carcinomas in males in the second study, with 4, 4, 6, and 18 (8%, 8%, 12%, and 25%) of the males in the 0.5, 2.5, 15.0 and 126 mg/kg dose groups respectively having this finding compared to 3 (6%) in the control group. A rare stomach tumor (an undifferentiated sarcoma) was found in a 2.5 mg/kg male and it is considered biologically significant in view of its occurrence in several animals at the 126 mg/kg dose level in the second study. No stomach tumors were observed in control animals in any of these chronic rat studies. Several primary brain tumors were noted in treated animals in both the earlier chronic rat study and in the 126 mg/kg dose level extension of the more recent study. The brain tumors observed in the first study were classified as ependymomas, whereas several neuroepitheliomas were observed in the second study. The increased incidences were not significant compared to the control groups. However, the registrant has concluded that these tumors "were possibly due to, or secondary to, treatment with the compound", apparently due to the rarity of this tumor in Long-Evans rats. Although the incidence of ependymoma does not appear to be compound-related, the Agency has not yet concluded whether the incidence of neuroepithelioma is biologically significant and has requested historical control data from the registrant regarding the incidence of this tumor type.

Epichlorohydrin (ECH), when tested alone, has been shown to induce both nasal turbinate tumors and stomach tumors in rats (Laskin, 1980; Konishi, 1980). These ECH-associated nasal turbinate tumors appear to be of similar histogenic origin as the ones noted in the alachlor rat studies. The ECH-associated stomach tumors were not malignant, in contrast to those observed in the studies with alachlor. It is difficult to estimate the contribution, if any, ECH made to the results observed in the rat and mouse studies due to the following:

- The rats were of different strains in the alachlor and ECH studies.
- ECH was administered through different routes of exposure (i.e. inhalation exposure (Laskin, 1980); oral exposure through treated water (Konishi, 1980); and oral exposure through treated feed (Daly, 1981b).
- ECH was administered to the animals for different durations.

However, the occurrence of these same tumor types in the second rat study in which a different stabilizer replaced ECH (and its 126 mg/kg/day dose extension), demonstrates an alachlor related effect, independent of ECH.

7. Human Studies

The Agency is unaware of any human studies that have investigated the oncogenicity of alachlor. There is one limited epidemiological study which investigated the ocular status of workers in a plant where alachlor was manufactured (Coleman, 1980) but no attempt was made to address oncogenic effects in this study.

8. Weight-of-the-Evidence

The goal of the Hazard Identification step of the Cancer Risk Assessment is to reach a qualitative judgment on the evidence that alachlor may be a human carcinogen.

The data in Table 4 show that alachlor has demonstrated statistically and biologically significant oncogenic responses at multiple sites at multiple doses in two sexes of one rodent species and at one site at one dose in one sex of a second species. Several oncogenic observations were replicated in the rat (see Table 3).

Table 4. Summary of Statistically Significant Oncogenic Responses in Alachlor Feeding Studies in Mice and Rats.

Mouse	Rat
Lung--at one dose (F)	Nasal turbinates--at three doses (MF)[1]
	Stomach--at one dose (MF)[1]
	Thyroid--at one dose (M)[1]
	Thyroid--at one dose (F)

1/-- Seen in more than one study.

All observed stomach tumors were malignant as were several of the tumors observed at other sites. In addition, the incidence of nasal turbinate tumors observed after two years in rats exposed for 5 to 6 months demonstrates that less than lifetime exposure is sufficient to elicit an oncogenic response in rats (Stout, 1983b).

As further supporting evidence, it can be noted that alachlor is structurally similar to another substituted acetanilide (metolachlor) which has demonstrated oncogenic effects (neoplastic nodules of the liver (NAS, 1980)) in the Sprague-Dawley strain of rat. Mutagenicity tests of alachlor have produced negative results (with the possible exception of the recently submitted DNA hepatocyte repair study which indicated DNA repair activity at the highest dose tested), but the Agency is requesting additional genotoxicity data derived from a broader range of test systems.

The Agency concludes that alachlor is a demonstrated animal oncogen. There are no data available concerning direct evidence of oncogenic effects in humans. Therefore, the Agency takes the position that alachlor should be viewed as having the potential to be a human oncogen. In the context of the categorization adopted by EPA modification of the IARC classification scheme (EPA, 1984), alachlor would be assigned to category B2, a probable human carcinogen.

B. Dose-Response Assessment

The upper bound estimates of excess cancer risk presented in this document are based on extrapolation from tumor rates in both males and females in the second rat oncogenicity study without the high dose (i.e. using doses 0, 0.5, 2.5, and 15 mg/kg (Stout, 1983a)). The reasons for this choice and the effect of including other available data sets are discussed below. Extrapolation is done using the linearized multistage model (computed by the Global 83 computer program). This is in keeping with Agency policy for those chemicals for which information regarding the mechanism of oncogenicity is unknown. Also in keeping with Agency policy, the interspecies extrapolation for oncogenic effects is accounted for by expressing the dose in terms of weight of alachlor per body surface area per day, rather than weight per body weight per day (EPA, 1984). The effect of treating interspecies differences this way is to increase the experimental rat estimate of risk approximately five fold in humans.

The mouse oncogenicity study is not being used for quantitative risk assessment purposes because the tumor types observed in the chronic rat studies (nasal turbinate, stomach and thyroid) are considered to be more reliable predictors of oncogenic potential than the mouse lung tumor (IARC, 1983). Furthermore, the oncogenic responses in the rat were observed in two separate studies reviewed by the Agency.

Because tumors in rats were observed at several sites in both sexes of two separate studies, there were a large number of possible approaches to a quantitative risk assessment. The result of using various data sets and combinations are shown in Table 5. The Q_1^* is a parameter of the linearized multistage extrapolation model. It is used as a multiplier of the estimated exposure (in units of mg/kg/day) to obtain the estimated 95% upper bound on risk. A change in the Q_1^* will result in a proportional change in risk.

The entries of Table 5 show that the choice of the data set from among those available for rat oncogenicity makes little difference in the risk estimate. With one exception, the range of the Q_1^*s shown in that table is less than an order of magnitude.

The Q_1^*'s actually used to produce the upper bound risk estimates are 5×10^{-2} (for male nasal turbinate tumors in the second study without the high dose) and 1×10^{-1} (for the corresponding data set for females.) Several other possible approaches were carefully considered by the Agency and are also discussed in this section.

- The Agency's proposed Guidelines for the Evaluation of Oncogenicity (EPA, 1984) recommend pooling the incidence of tumors showing significant elevations for quantitative risk assessment purposes. In the case of the data set used for extrapolation (second study without the high dose), the pooling of tumors results in a change in the status of only one animal, a male rat with a stomach tumor at the 2.5 mg/kg dose. The change in the status of this animal caused an increase in the Q_1^* from 5×10^{-2} to 1×10^{-1} for males (see Table 5). The very fact that this two-fold change resulted from a change in status of only one animal illustrates the instability of quantitative risk estimates within a twofold range. This range is well within the uncertainty generally associated with all risk assessments. It is also within the range of Q_1^*'s used for the risk estimates presented in this document. Therefore, using pooled tumor types would have virtually no effect on the risk estimates.

- The first alachlor rat study provided results qualitatively similar to those produced in the second study. The two studies differed quantitatively, however, as discussed in Chapter II.A.6. The second study is considered the more appropriate for risk assessment because it was conducted with the current technical alachlor mixture and because it was designed and conducted with knowledge that nasal tumors were likely. The Agency considered combining the results of these two studies and the effect of doing so is shown in Table 5. The range of upper bound risk estimates would vary less than two-fold from the range given in the risk tables presented in this document. Since the upper bound risks are presented as order of magnitude ranges, this degree of difference makes no meaningful difference in the risk ranges discussed in this document.

- As previously noted, the additional dose level (126 mg/kg) was used in the second chronic rat study for the purpose of investigating the reversibility of eye lesions previously observed in the earlier rat study. Because of the criterion employed in assigning animals to the various subgroups in this study (discussed in Chapter II.6. of this document), this dose level is not considered fully appropriate for quantitative risk assessment. However, if it were included, the effect would be a slight increase the Q_1^* for males and a decrease for females (less than two-fold), leaving a range similar to, but somewhat less than that actually used by the Agency. As discussed above, this variation is well within the range of uncertainty generally associated with quantitative risk assessment.

Table 5 also illustrates the effect of combining or separating the tumor incidences observed in males and females.

Table 5. Q_1^* Potency Estimates for Alachlor Based on Rat Tumor Data

Nasal Turbinates					Turbinates, Stomach or Male Thyroid (Follicular Ad/Ca)			
		Combining Sexes					Combining Sexes	
Males	Females	Program InPut	Geometric Mean	Study Data	Males	Females	Program Input	Geometric Mean
4×10^{-2}	1×10^{-2}	2×10^{-2}	2×10^{-2}	First Study	3×10^{-3}	2×10^{-2}	2×10^{-2}	2×10^{-2}
9×10^{-2}	7×10^{-2}	8×10^{-2}	8×10^{-2}	Second Study	1×10^{-1}	1×10^{-1}	1×10^{-1}	1×10^{-1}
5×10^{-2}	1×10^{-1}	6×10^{-2}	8×10^{-2}	Second Study without High Dose	1×10^{-1}	1×10^{-1}	9×10^{-2}	1×10^{-1}
6×10^{-2}	3×10^{-2}	4×10^{-2}	4×10^{-2}	Combined Studies	6×10^{-2}	4×10^{-2}	5×10^{-2}	5×10^{-2}
5×10^{-2}	2×10^{-2}	3×10^{-2}	4×10^{-2}	Combined without second study High-Dose	5×10^{-2}	4×10^{-2}	4×10^{-2}	5×10^{-2}

The combination of data for sexes may be done in either of two ways. First, when data sets for both sexes are essentially equivalent, the data sets are entered together into the computer program and the combined result yields a flattened slope as a result of the increased sample size. Second, when there is some meaningful difference in the dose response patterns displayed by the sexes, the calculation of the geometric mean of two or more Q_1*s is appropriate. Table 5 presents potency estimates using both of these approaches for each data set (program input and geometric mean, respectively).

Table 5 thus illustrates 40 different approaches to the risk extrapolation from the chronic rat studies to man. It can be readily seen from Table 5 that the use of other subsets of the data yield potency estimates which are similar to that derived from the use of the second chronic study excluding the 126 mg/kg dose level. For example, potency estimates derived from both studies and all dose levels combined are 6×10^{-2} (males) and 3×10^{-2} (females). In fact, all potency estimates are within a fairly narrow range.

The risk tables which follow in this document present the range of upper bound estimates of excess cancer risk generated by extrapolation from tumor rates for both males and females in the second rat oncogenicity study without the high dose (i.e. using doses of 0, 0.5, 2.5 and 15 mg/kg). The upper end of the range represents extrapolation from nasal turbinate tumors in females as well as extrapolatyion from the combined tumor totals (nasal turbinate, thyroid and stomach) of either sex, i.e. these approaches yield identical potency estimates. The lower end of the range represents extrapolation from the incidence of nasal turbinate tumors observed in males.

C. Exposure Assessment

The principal routes of exposure to alachlor for the general population are via the diet and drinking water. Exposure to users and applicators are also examined below.

1. Dietary Exposures

a. Residues from Treated Raw Agricultural Commodities

Alachlor is registered primarily for preemergence use on beans (dry), corn, cotton, lima beans, peanuts, peas, sorghum, soybeans, sunflowers, and woody ornamentals. Tolerances for alachlor have also been established for eggs, milk, and the fat, meat, and meat byproducts of cattle, goats, hogs, horses, poultry, and sheep. The residue levels permitted under the alachlor tolerances include residues of alachlor per se plus selected metabolites.

The metabolism of alachlor in plants is generally understood. Residue data indicate that alachlor is absorbed by corn, cotton, peanut, and soybean plants from treated soil (Monsanto, 1967 and 1969). Data from a ^{14}C labeled metabolism study in plants indicate residues are translocated throughout the entire plant. However, a recent ^{14}C labeled metabolism study (Monsanto, 1983b) indicated that only 10% and 8%, respectively, of the total soybean ^{14}C foliar and bean residue may be detectable by the analytical method presently used for enforcement purposes (Kovacs, 1984). The enforcement method may detect only those residues which are converted to 2,6-diethylaniline following the acid hydrolysis step. In the same study, 50% and 30%, respectively, of the total soybean foliar and bean ^{14}C residue was discovered to be converted to 2-ethylaniline following acid hydrolysis. The remaining activity was either unextractable, unidentified or arose from radioactive impurities in the applied dose. None of the latter residues have been shown to be detectable by the current enforcement methodology. For these reasons the registrant has been required via the Registration Standard to furnish data which demonstrate the ability of the present enforcement method to detect metabolites convertible to 2-ethylaniline or, if that is not possible, to develop an analytical methodology which could determine metabolites of alachlor that can be converted, following acid hydrolysis, to 2-ethylaniline in addition to those converted to 2,6-diethylaniline (Zager and Loftus, 1984).

In light of the limits of the present methods of analyzing for significant levels of alachlor metabolites, the actual measured residue levels and/or the tolerances established to limit the maximum residue level may be lower than appropriate.

The metabolism of alachlor in domestic animals is not well understood at this time and the levels of residues of concern in domestic animals and their byproducts cannot be fully ascertained. In particular, it has not been demonstrated whether the residues in animals do indeed contain only the 2,6-diethylaniline moiety. The previously submitted cattle and swine feeding studies were conducted at IBT and are considered invalid. In the recently submitted goat and laying hen $^{13}C/^{14}C$ labeled feeding studies (Monsanto, 1984b and 1984c), the identity of the residues was not determined. In addition, the reliability of the studies is questionable. The data reflect only one feeding level (5.4 ppm for goats and 9.2 ppm for hens) and a short duration of feeding (5 days for goats, 6 days for hens) (Dodd, 1984a and 1984b). Therefore, animal metabolism/feeding studies using both poultry and ruminants have been required as a condition for any period of continued registration and are expected to be submitted in the fall of 1984.

The maximum expected dietary intake of alachlor residues by poultry and swine is 0.2 ppm of alachlor in feed based on the consumption of corn grain and soybean meal in any combination. Based upon the available information, the maximum expected dietary intake of alachlor by cattle (meat and dairy) would be 3 ppm if the diet consisted solely of peanut forage and hay. A more realistic diet would consist only of 60% peanut hay and 40% corn grain which would result in a maximum expected dietary intake of 1.9 ppm. These estimates of alachlor residue levels are based on the detection of parent compound and the metabolites containing the 2,6-diethylaniline moiety only. Recently submitted plant metabolism studies indicate that a significant portion of plant residues, particularly in soybeans, consist of metabolites convertible upon acid hydrolysis to 2-ethylaniline. Therefore, estimated dietary intakes may actually underestimate livestock's dietary burden. In any event, these dietary burdens cannot be extrapolated to residues in meat and milk without adequate analysis of the metabolism of alachlor (and its metabolites) in the animal. In addition, the enforcement method does not appear to detect residues convertible to 2-ethylaniline. The metabolites convertible to 2-ethylaniline are significant in plants and may be important in meat, milk, poultry and eggs as well.

Estimates of dietary exposure are presented in the following table using the standard EPA "food factor" system to estimate levels of each food item in the typical diet (Schmitt, 1977). The first column in Table 6 indicates dietary exposure assuming that all commodities contain residues of alachlor at the tolerance level. The second column presents dietary exposure for corn, beans, peas, potatoes, cottonseed and peanuts using the best available estimate of residues which are the maximum reported residue levels from actual field trials reflecting the maximum registered use rates (currently up to 8 lbs/acre) and are, in most cases, less than the tolerance levels. These residue levels are the maximum observed residues using the present enforcement method of analysis. The Agency recognizes that the actual use rates are frequently less than the maximum registered use rates. However, the available data do not indicate lower residues resulting from lower than maximum use rates. Due to the lack of appropriate data for sunflowers, sunflower seeds are assumed to contain residues at the tolerance level. As explained above, these estimates do not include residues convertible to 2-ethylaniline upon acid hydrolysis and thus may underestimate the actual dietary exposure to alachlor and relevant metabolites.

Table 6. Dietary Exposure to Alachlor and Metabolites Convertible to to 2,6-Diethylaniline Upon Acid Hydrolysis

Crop	Theoretical Maximum Residue Contribution		Best Available Estimate	
	Tolerance (ppm)	Dietary Exposure (mg/kg/day)	Tolerance or Actual Residue	Dietary Exposure (mg/kg/day)
corn	0.20	1×10^{-4}	0.05	3×10^{-5}
soybeans	0.20	5×10^{-5}	0.09	2×10^{-5}
beans (dry, edible)	0.10	8×10^{-6}	0.09	7×10^{-6}
beans (Lima)	0.10	5×10^{-6}	0.08	4×10^{-6}
peas	0.10	2×10^{-5}	0.10	2×10^{-5}
potatoes *	0.10	1×10^{-4}	0.08	1×10^{-4}
cottonseed oil	0.05	2×10^{-6}	0.02	7×10^{-7}
peanuts	0.05	5×10^{-6}	0.02	2×10^{-6}
sorghum	0.10	8×10^{-7}	0.05	4×10^{-7}
sunflower seed	0.25	2×10^{-6}	0.25	2×10^{-6}
milk & dairy	0.02	1×10^{-4}	0.02	1×10^{-4}
meat & poultry	0.02	7×10^{-5}	0.02	7×10^{-5}
eggs	0.02	1×10^{-6}	0.02	1×10^{-6}
TOTAL		6×10^{-4}		4×10^{-4}

* The potato use has been discontinued. Removal of the the contribution from potatoes would reduce the total TMRC to 5×10^{-4} mg/kg/day and the total Best Available Estimate to 3×10^{-4} mg/kg/day.

EPA has evaluated dietary exposure using the more sophisticated assessment of dietary behavior contained in the Tolerance Assessment System (TAS). The new system was described in the Agency's "Ethylene Dibromide (EDB) Scientific Support and Decision Document for Grain Milling and Fumigation Uses" on February 8, 1984. The estimates used in the system rely on an extensive data base including the individual 3-day dietary behavior of 30,770 persons surveyed by the U.S. Department of Agriculture. For the typical United States consumer, use of the TAS assessment method did not substantially alter the estimated dietary exposure.

TAS also permits estimation of dietary burdens of alachlor from treated crops for population subgroups, as shown in Table 21 (see Chapter II.D.1.a. These estimates utilize the best available residue estimates in contrast to the use of the tolerance limit in every use. The average for the total (48 state) population is only slightly different from the corresponding estimate based upon the standard food factors.

Analysis of dietary exposure patterns using the new TAS indicates a relatively uniform distribution to the general population which suggests that a large number of individuals have similar exposure patterns. This is borne out in the examination of data for various subgroups which indicates similar exposure patterns for each region, ethnic group and season. However, there are important differences in exposure with respect to the age subgrouping. This table shows non-nursing infants to have the highest dietary burden. Children less than 12 years old are also found to have greater than average exposure. The infant diet (which contains a high proportion of soybean products) obviously lasts for only a short portion of any individual's lifetime. The risk estimate which assumes lifetime exposures associated with that diet must therefore be regarded as a worst case.

b. Exposure Through Drinking Water

The Agency is concerned about the finding of alachlor in both surface waters and ground water which are the sources of drinking water. These findings, particularly the occurrence of alachlor in municipal water supplies in Ohio, reflect an additional source of human exposure to alachlor.

Alachlor can enter water systems either by runoff from agricultural fields into surface water or by leaching downward through soil to ground water. Although alachlor is biologically degraded in soil, it does not readily degrade once it reaches aquatic systems. The tendency for alachlor to leach is lessened because of biological degradation in soil, but in areas with little biological activity or with fast recharge to ground water, such as through fractured soil, alachlor may be transported to ground water aquifers.

The U.S. population of about 231 million people obtains its drinking water from either public or private water supplies, which are derived from both ground and surface water sources. Public water supplies provide water for between 191 to 217 million people and 66% of these people use drinking water from surface water sources such as rivers, lakes, and reservoirs and 34% from ground water. The rest of the population, which does not use public water supplies, obtains drinking water primarily from private wells.

I. Exposure through Drinking Water from Ground Water Sources

The likelihood that an agriculturally-applied pesticide will leach below the unsaturated root zone to the saturated zone and eventually appear in ground water and drinking water is dependent on several factors. Two important factors involve the persistence and mobility of the pesticide. The rate of decay in the soil environment is obviously important; the more rapidly decaying pesticides are less likely to leach than do the more persistent pesticides. Solubility and the soil binding nature of a pesticide are also important in determining its potential to leach. A common measure of the latter is the soil partition coefficient, K_d, which is the ratio of pesticide quantity adsorbed to soil to that quantity dissolved in water.

In a recent comprehensive review of the leaching of agricultural pesticides to ground water, Cohen et al. (1984) concluded that pesticides have a potential to leach when the soil half-life is greater than 2-3 weeks, the solubility is greater than 30 ppm, and the K_d is less than 5. For alachlor, soil half-life values are in the neighborhood of 3 weeks, the solubility is 240 ppm, and reported K_d values are in the range of 0.6-8.1, depending on soil type, with most values less than 4.0. Pesticides applied to sandy soils have a much greater chance of leaching for two reasons: more water leaches through a sand soil than through other soil types, and K_d values of pesticides on sand are typically lower due to low organic matter and low clay content for binding sites.

The method of application is also an important factor of leaching. Soil incorporation tends to increase the leaching potential relative to surface or foliar application. Other factors include soil and air temperature (pesticides which biodegrade do so more slowly in cooler temperatures), rainfall near the time of application, geography (weather and soil patterns), and rate of pesticide application.

Table 7 summarizes available data on alachlor found in ground water. The data show that alachlor has been found in well water at levels ranging from 0.01 to 16.6 ppb in three states and in Ontario, Canada. Higher levels observed in

Ontario (Frank, 1984) were determined to be the result of spills. Areas tested in Nebraska were known to have sandy soils and shallow, unconfined aquifers, and to be corn-growing areas (Spalding et al, 1984). The route to wells in the three Iowa counties was through normal infiltration and also through runoff and interflow to karst sinkholes followed by rapid infiltration.

Mathematical models can be used to predict pesticide transport through the unsaturated zone to the saturated zone and to determine the potential of a pesticide leaching and eventually contaminating ground water. One such model is the Pesticide Root Zone Model (PRZM), which was developed at the U.S. EPA Environmental Research Laboratory in Athens, Georgia (Carsel et al., in press). It is a one-dimensional, time-varying model for evaluating pesticide fate and transport in the unsaturated soil zone. A field validation study was initiated in 1983 by EPA to evaluate the ability of PRZM to predict actual pesticide movement through soils. The five-year study will collect field data of pesticide leaching for comparison to model predictions.

Table 7. Summary of Data on Alachlor in Wells

Location	$\frac{\text{Positive Samples}}{\text{Total}}$	Conc.(ppb):mean positives,range	Comments
Ontario, Canada (Frank, 1984)	$\frac{10}{28}$	2.1, 0.01-9.1	rural well water; 1979-1984 tests; all positive wells were shallow
Ontario, Canada (Frank, 1984)	$\frac{8}{153}$	147, 0.6-780.0	rural well water 1979-1984 tests; 7 of 8 were result of spills
Nebraska (Spalding et al., 1980)	$\frac{2}{14}$	.04, .018-.071	Central Platte Region; 1-2 m silt loam above sand and gravel; nitrate found
Devonian-Carbonate Aquifer, Floyd and Mitchell Co. Iowa(Libra et al., 1984)	8/93	8.3, 0.10-16.6	major findings in Incipient Karst well; water level is 3-5 m below surface
Big Spring Basin, Clayton County, Iowa (Hallberg et al, 1983)	3/35	.09, 0.05-0.15	groundwater discharge into Big Spring
	1/59	.05	study area wells
	4/5	5.1, 0.3-12.7	surface water draining into sinkholes
Maryland (Maryland DHMH, 1983)	4/30	0.4, 0.1-0.8	wells located in agricultural areas reflecting statewide distribution

The PRZM model was utilized in two ways to determine the leaching potential of alachlor. In one, the methodology known as LEACH (Leaching Evaluation of Agricultural Chemicals: A Handbook) was used (Dean et al.,1984). In LEACH, the potential for leaching is expressed as the percentage of applied pesticide which leaches below the root zone of the crop plotted against percentage of time. Results of this exercise are found in Table 8.

The methodology uses PRZM runs simulating 25 years of use in 11 geographical regions (seven corn sites and four soybean sites). An important factor in evaluating these results is that the root zone for corn is 90 cm deep and the root zone for soybeans is 45 cm; alachlor would have to travel twice as deep to leave the corn root zone in contrast to the soybean root zone. Alachlor showed little potential to leach below the root zone in corn sites. The greatest potential for such migration was shown in Site 13, which is represented by South Carolina, but also encompasses North Carolina and Georgia. As much as 3% of applied alachlor is predicted to leach 10% of the time (or 1 year in 10). Site 13 was the southernmost site, and this result reflected the greater amounts of rainfall and the more intense spring rainfalls in the South as compared to the North. Soybean sites showed more potential for leaching, although again this was due to the shallower root depth of soybeans. Sites 15 and 17, again in the southernmost states, showed the most potential. In Site 15, as much as 8% of the applied would leach 10% of the time, and, in Site 17, as much as 15% of the applied would leach 10% of the time.

The second exercise involved the use of PRZM itself to evaluate the leaching potential of alachlor when applied to corn in Iowa and soybeans in Indiana. As seen in Table 9, PRZM simulations on corn and soybeans showed results comparable to LEACH results. Less than 0.01% of the applied alachlor was predicted to leach below the corn root zone in Iowa, but the simulation predicted that 4.6% would leach below the soybean root zone. However, less than 0.01% was predicted to leach below two meters for either crop.

The PRZM model assumes a horizontally uniform soil profile. It cannot simulate the occurrence of leaching through sinkholes, fractured clay layers, or other heterogeneous soil horizons. Monitoring data verify that these features can significantly affect the occurrence of pesticide residues in ground water.

In summary, it can be stated that alachlor has demonstrated a potential to leach. As seen in Table 7, alachlor has been found in wells, and the causes of these findings have ranged from accidental spills to seepage through sinkholes to infiltration through soil from normal agricultural use. Further, model simulations with the PRZM model show that alachlor has the potential to leach below soybean root zones, and to a lesser extent, below corn root zones, which reinforces the limited monitoring data.

Table 8. Results of LEACH Analysis
Percent of Applied Alachlor Estimated
to Leach Below Root Zone*

Site	Representative State	Percent of applied alachlor leaching below root zone for listed percent of time 5%	10%	50%
I. Corn				
7	CO	1-2	<1	0
8	NE	0	0	0
9	IL	<1	0	0
10	MI	1	<1	0
11	OH	1	1	<1
12	MD	2-3	1-2	<1
13	SC	1-3	1-3	0-1
II. Soybeans				
14	IA	1-5	1-4	0-2
15	MS	5-9	4-8	3-5
16	IN	3-5	2-4	1-3
17	SC	6-18	5-15	4-8

* corn root zone = 90 cm; soybean root zone = 45 cm

Table 9. Summary of PRZM Results for Alachlor Applied to Corn in Iowa and Soybeans in Indiana

Description	Corn - Iowa	Soybeans - Indiana
1. Percent of applied alachlor leaching below root zone, %	<0.01	4.6
2. Percent of applied alachlor leaching 2 meters, %	<0.01	<0.01
3. Average peak soil water concentration of alachlor at 2 meters, ppb.	<0.5	<0.5

II. Exposure through Drinking Water from Surface Water Sources

A. Monitoring Data

Monitoring data for alachlor in surface water are shown in Tables 10 and 11. Table 10 contains a summary of monitoring data extracted from a number of reports which are referenced in the table. In addition, Table 11 contains a summary of alachlor monitoring data extracted from the STORET data base, a publicly-accessible data base maintained by EPA (U.S. EPA, 1982). Alachlor concentrations in drinking water (tap water) are shown in Table 12.

The mean concentration (ppb) was calculated as a simple arithmetic mean of all samples. An individual sample was either a daily sampling or one of multiple samples collected in a day. The value of 0.00 was assigned to samples where alachlor concentration was less than the limit of detection of the analytical method. Generally, the limit of detection of the analytical method for alachlor in water is 0.15-0.25 ppb, although lower limits have been obtained in individual studies. The mean concentration is not necessarily an average daily or seasonal exposure, but simply an average of the measurements which were taken.

To highlight some of the data, surface water monitoring studies in several rivers in northwestern Ohio show the presence of alachlor at all sampling stations at most of the sampling times, which were during the summer months of 1981-1984 with peak concentrations occurring consistent between late May and early June. The areas where these monitoring studies were carried out are dominated by corn and soybean production. In general, the highest pesticide concentrations were found in the rivers during the first major runoff events following spring planting. The findings of alachlor residues in surface waters two months after spray-time applications is evidence that alachlor persists in streams or persists in fields for subsequent runoff.

In 1983, simultaneous monitoring of the Maumee and Sandusky rivers and tap water from three municipal water supplies deriving their water from these rivers showed average alachlor levels of 1.24 and 3.11 ppb in the rivers and 0.22, 1.08 and 1.87 ppb in tap water during the period from May 28 to July 27. The data indicate that alachlor is not removed by conventional water treatment processes which do not include carbon filtration. Less than 1% of the wells, both public and private, which supply drinking water in the United States are equipped with carbon filtration. None of the municipal water supply systems in the United States are equipped with carbon filters, although some use activated carbon powder for removal of disagreeable taste and odors.

The peak concentrations in surface water (e.g., 267.7 ppb at Four-Mile Creek (Iowa) Watershed Site #4 and 104.6 ppb at Defiance) were accountable to runoff events. High pesticide concentrations in runoff are due to high soil-moisture content of soil at the site during rain following the application of alachlor in the spring and summer months. The concentration of alachlor in runoff depends on the intensity and magnitude of rainfall and amount of alachlor present in the field during a rainy day.

Table 10. Alachlor in Surface Water

State	Sampling Site	# Positive / Total	Peak Conc. (ppb)	Date of Peak Conc.	Mean Conc. (ppb)[1/]	Sampling Period
OH(1981) (Baker et al, 1981)	Honey Creek, Melmore	121/158	57.0	6/9	5.48	3/30/81-9/7/81
	Honey Creek, Tiro	4/5	3.87	6/9	1.13	6/9/81-9/7/81
	Upper Honey Creek	42/46	75.6	6/9	10.08	5/4/81-/9/7/81
	Bean Creek, Powers	8/12	32.7	6/9	3.79	3/31/81-7/7/81
	Ottawa River, Allentown	5/10	14.2	6/16	3.18	3/31/81-7/7/81
	Rocky River, Berea	1/5	0.035	5/20	0.01	3/31/81-5/20/81
	Sandusky River, Tindell	16/17	42.5	6/11	10.29	5/26/81-9/7/81
	Sandusky River, Mexico	2/2	0.455	9/7	0.30	6/4/81-9/1/81
	Sandusky River, Defiance	28/30	104.6	6/8	10.94	5/29/81-7/6/81
	Wolf Creek, East Br	3/3	67.7	6/9	29.26	6/9/81-6/14/81
	Wolf Creek, West Br	3/3	54.1	6/9	27.74	6/9/81-6/14/81
	Maumee River, Waterville	1/1	6.97	6/16	-	6/16/81
OH(1982) (Baker, 1983b)	Maumee, Bowling Green (6,313 mi^2)	45/53	9.27	5/28	1.88	12/8/81-8/23/82
	Sandusky, Fremont (1,251 mi^2)	45/51	18.19	5/29	4.16	12/7/81-8/23/82
	Raisin River, Monroe, Mi	21/25	8.16	5/29	1.71	4/5/82-8/28/82

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[1] A value of 0.00 was assigned to samples where alachlor was not detected. The mean concentration is a simple arithmetic mean of all samples analyzed.

Table 10. Alachlor in Surface Water (cont'd)

State	Sampling Site	# Positive / Total	Peak Conc. (ppb)	Date of Peak Conc.	Mean Conc. (ppb)[1]	Sampling Period
	(1,042 mi^2)					
	Honey Creek, Melmore (149 mi^2)	56/65	75.0	5/24	7.99	12/7/81-8/23/82
	Cuyahoga (707 mi^2)	8/24	0.60	7/19	0.07	12/7/81-8/23/82
OH(1982) (Baker, 1983b)	Lost Creek, Defiance (4.4 mi^2)	41/51	18.46	5/22	0.83	12/8/81-8/23/82
OH(1983) (Baker, 1983b)	Sandusky, Fremont (1,251 mi^2)	-	-	-	1.24	5/28/83-7/27/83
	Maumee, Bowling Green (6,313 mi^2)	-	-	-	3.11	5/28/83-7/27/83
OH(1984) (Baker, 1984b)	Rock Creek	40/54	7.42	5/21/84	1.21	4/3/84-7/24/84
	Maumee River, Bowling Green	43/52	18.35	5/24/84	4.38	4/2/84-7/30/84
	Sandusky River, Fremont	46/54	9.10	6/28/84	2.22	4/2/84-7/30/84
	Sandusky River Defiance	35/39	33.11	5/21/84	4.58	4/2/84-7/30/84
	Honey Creek, Melmore	57/65	22.89	7/7/84	2.92	4/2/84-7/30/84
	Raisin River	13/17	5.03	5/27/84	0.70	4/8/84-7/29/84
	Cuyahoga River (urban watershed)	5/14	0.35	7/23/84	0.07	4/24/84-7/23/84

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[1] A value of 0.00 was assigned to samples where alachlor was not detected. The mean concentration is a simple arithmetic mean of all samples analyzed.

Table 10. Alachlor in Surface Water (cont'd)

State	Sampling Site	# Positive / Total	Peak Conc. (ppb)	Date of Peak Conc.	Mean Conc. (ppb)1/	Sampling Period
(Miltner, 1984)	Sandusky River, Tiffin	17	13.7	6/27/84	5.4	5/21/84-7/9/84
	Sandusky River, Fremont	7	5.5	5/21/84	3.4	5/18/84-6/25/84
	Maumee River, Bowling Green	20	12.2	5/25/84	3.6	5/15/84-7/16/84
OH (Columbus) (Binder, 1984: Raw Water Intake)	Dublin Road, water plant(raw)	8/8	5.71	6/30/81	1.19	6/30/81-1/11/82
	Dublin Road water plant(raw)	11/11	6.10	6/11/82	3.18	6/10/82-7/21/82
	Dublin Road water plant (raw)	7/7	3.65	7/14/83	3.23	7/14/83-8/16/83
	Dublin Road water plant					
	DRWP Intake	4/4	0.45	1/82	0.26	10/81-1/82
	Griggs Reservoir	4/4	0.48	1/82	0.31	10/81-1/82
	Griggs Reservoir	3/3	5.76	6/26/83	2.14	6/26/83-8/29/83
	O'Shaughnessey Reservoir	4/4	0.51	1/82	0.37	10/81-1/82
	O'Shaughnessey	3/3	5.07	6/26/83	1.84	2/12/83-8/29/83
	Morse Road water plant					
	MRWP Intake	4/4	0.25	10/81	0.20	10/81-1/82
	Alum Creek Reservoir	4/4	0.52	10/81	0.42	10/81-1/82
	Alum Creek Reservoir	3/3	0.95	6/26/83	0.79	2/12/83-8/29/83
	Hoover Reservoir	4/4	0.40	10/81	0.35	10/81-1/82
	Hoover Reservoir	3/3	0.41	8/29/83	0.35	2/12/83-8/29/83
	Other Samples					
	Bokes Creek	1/1	7.83	6/22/83	-	6/22/83
	O'Shaughnessey Top	1/1	4.05	6/27/83	-	6/27/83
	O'Shaughnessey Bottom	1/1	6.33	6/27/83	-	6/27/83
	O'Shaughnessey LLYC	1/1	3.57	6/26/83	-	6/26/83
IA (Johnson et al., 1982,	Four Mile Creek Watershed Site 4	27/145	9.60	5/29/76	1.77	5/2/76-9/19/76
		4/86	0.30	5/22/77	0.01	4/10/77-10/1/77
		45/130	54.50	6/19/78	2.32	5/1/78-9/14/78
		205/222	267.70	6/4/79	5.55	5/1/79-10/29/79
		101/104	208.70	6/15/80	20.27	5/8/80-8/11/80
Clayton County (Hallberg et al., 1983)	Big Spring (surface water)	9/9	20.00	6/8/82	2.86	2/24/82-12/29/82

Table 11. Alachlor in Surface Water
Stations Reporting Alachlor Greater Than 2 UG/L in STORET

State	Sampling Site	Positive/Total	Peak Conc. (ppb)	Date of Peak Conc.	Mean Conc.* (ppb)	Sampling Period
AR	Little River	7/39	2.1	6/9/76	0.08	3/76-10/82
IO	Chariton River	22/28	101.0	7/19/78	12.58	5/78-7/78
KS	Big Blue River	13/25	3.2	6/16/82	0.68	6/78-9/83
	Marmaton River	1/5	4.2	7/7/82	0.91	7/79-7/83
	Walnut River	1/16	2.4	12/19/82	0.25	12/78-10/78
	Wakarusa River, below Clinton Dam	1/9	3.2	5/7/78	0.25	1975-1978
	Wakarusa River near Topeka	0/3	0.0	--	0.0	9/82-9/84
	Soldier Creek	1/18	4.4	7/13/82	1.87	4/79-7/83
MD	Octoravo Creek	4/4	2.7	6/4/81	--	6/81-9/81
MI	Raisin River	21/23	8.2	5/29/82	1.86	4/82-8/82
OH	Maumee River	47/51	9.3	5/28/82	1.99	12/81-8/82
	Sandusky River	45/49	18.0	5/29/82	4.43	12/81-8/82
	Honey Creek	56/60	70.0	5/25/82	5.93	12/81-8/82
PA	West Conewago Creek	4/4	11.0	6/4/81	3.92	6/81-9/81
VA	Blackwater Creek	1/1	3.4	5/23/79	2.0	5/79

* A value of 0.00 was assigned to samples where alachlor was not detected. The mean concentration is a simple arithmetic mean of all samples analyzed.

Table 12. Alachlor in Tap Water

State	Sampling Site	Positive Total	Peak Conc. (ppb)	Date of Peak Conc.	Mean Conc. (ppb)	Sampling Period
OH	Tiffin (Ohio EPA, Baker 1983a)	6/6	14.0	5/25/82	4.14	5/10/82-7/7/82
	Tiffin (Baker et al 1981)	6/6	14.3	6/17/81	5.10	6/4/81-9/1/81
	Tiffin (Baker, 1982)	3/5	11.4	5/28/82	2.45	12/10/81-5/28/82
	Fremont (Baker, 1983b)	-	-	-	0.22	5/28/83-7/27/83
	Bowling Green (Baker, 1983b)	-	-	-	1.87	5/28/83-7/27/83
	Tiffin (Baker, 1983b)	-	-	-	1.08	5/28/83-7/27/83
olumbus Binder, 984)	Dublin Road water plant(tap)	6/6	1.10	8/3/81	0.47	6/30/81-1/11/82
	Dublin Road water Plant(tap)	11/11	5.71	6/11/82	2.82	6/1/82-7/21/82
	Dublin Road water plant(tap)	7/7	3.57	7/14/83	2.39	7/14/83-8/16/83
A Nat. es. Council, 977)	New Orleans City	-	2.9	1977 (Summer)	-	-

B. Modeling Assessment

In order to more fully understand the significance of the available data on alachlor contamination of surface drinking water sources, EPA has employed a model designed to predict pesticide concentrations in streams resulting from transport of the pesticide from field application sites to the stream. This model, the Hydrologic Simulation Program - Fortran (HSPF), takes into account the various processes which are likely to influence the behavior of alachlor in watershed areas, both on and in the soil and within the stream (Johanson, et al., 1980). The model was applied to predict the instream concentrations which would be expected in three watersheds where alachlor is applied to soybeans and corn. The watersheds reflect a range in the extent of alachlor use and in geographic and climatic conditions.

Sections 1 and II of Mulkey et al. (1984) provide a fuller discussion of the properties which influence the movement of alachlor in watersheds, and the methodology by which the HSPF model accounts for all the factors appropriate for useful predictions of pesticide concentrations in streams.

As noted above, HSPF was applied to data from three watersheds. The first, the Iowa River Watershed in central Iowa is located in the heart of the corn belt where about 67% of the land area is used to grow corn and soybeans. Alachlor is applied there in late May or early June. The heaviest rainfalls occur in those months, and annual rainfall is moderate (approximately 30 inches per year). In the second watershed, the Little River Watershed in south central Georgia, only about 20% is cropped to soybeans or corn, where alachlor is applied in mid-March. March, June, July and August are the wettest months; annual rainfall is heavier (approximately 45 inches). The third watershed, the Yazoo River is a major stream flowing into the Mississippi River. The watershed area used for this study contains about 31% corn and soybean land. Alachlor use occurs in April which, with December, is the wettest period. Intense periodic rainstorms and flooding are frequent and annual rainfall is about 52 inches.

The data and calibrations required for hydrologic simulation with the HSPF model are available for each of these specific watersheds. Such site-specific data for model simulations are rare. For alachlor, application rates and modes were taken from label directions and application times were assumed to be distributed through the time period normal for each area. Actual field data on pesticide disappearance rates and dissolved/non-dissolved partitioning were available from the Iowa area. Those data, supplemented by laboratory data as necessary, were used to model all three areas, with adjustments for known effects of temperature differences on the values. The values for acreage treated were based solely on corn and soybean acreage, because only those crops currently have extensive alachlor use. For the Iowa River Watershed, estimates of resulting instream concentrations were derived by three different approaches to estimate acreage treated using (1) the results of a site-specific alachlor use survey, (2) state-wide USDA use data, and (3) a "full treatment" hypothetical scenario that all corn and soybean acreage would be treated. In the Little River and Yazoo Watershed areas, only two approaches, regional USDA use data and the hypothetical "full treatment" case, were used. A fuller discussion of the data relied on for this modeling is contained in Section III and IV of Mulkey et al. (1984). With this HSPF simulation, it is possible to obtain estimates of instream concentrations at multiple points along the modeled stream length for any two-hour period over a ten-year span. Values for daily mean alachlor concentrations in the Iowa River are estimated for three locations; in the Yazoo River concentrations were estimated at two locations; and in the Little River only the concentrations at the mouth of the study area are estimated. The values for all of these areas were analyzed to determine the ten-year annual mean, the ten-year monthly mean in each of the spring/summer months which constitute the run-off season, and the ten-year peak daily mean for each year. Table 13 shows the three Iowa River locations, with annual estimates for each of the three treatment cases. Table 14 presents the ten-year averages for the two Yazoo sites, presented annually and by "high season" months for both treatment cases. Table 15 presents the ten-year average data for the Little River site. More complete results and a discussion of the results, including a comparison to available data on measured alachlor concentrations are found in Section V of Mulkey et al. (1984).

Several useful conclusions may be drawn from this modeling effort. In the Iowa River area, average concentrations over a ten-year period under current use patterns are predicted to be about 2 ppb. If all corn and soybean acreage in the area were treated with alachlor, the ten-year average would be greater than 5 ppb and in high rainfall years the average could reach 10-15 ppb averages for those years. The annual averages reflect months of zero concentration levels in the stream. Estimates of concentrations for individual "high season" months under current use patterns exceed 10 ppb with some frequency and can exceed 40 ppb. Daily concentrations are estimated to reach well over 200 ppb. Therefore, estimates of lifetime exposure based on alachlor contamination of surface water sources at 2-5 ppb appear realistic for the cornbelt area.

In the Yazoo and Little River areas, by contrast, ten-year average concentrations appear unlikely to exceed 1 ppb, even if all corn and soybeans were treated with alachlor. Some reaches of the Yazoo could see long-term average concentrations of from 1 to 2 ppb for a "full treatment" use pattern. Generally, estimates of lifetime exposure based on alachlor contamination of surface water outside the cornbelt area should not use values exceeding 1 ppb. "Worst case" estimates for the Yazoo might be appropriate using the 2 ppb average value possible in maximum rainfall years of full alachlor use.

For risk assessment purposes, these modeling estimates of alachlor concentrations greatly increase the confidence that the Agency can place in its estimates of drinking water exposure derived from the available monitoring data on alachlor contamination of surface drinking water sources and of tap water taken from those sources. The closeness between modeled and observed results, the opportunity to consider the effects of important variables such as rainfall or extent of use, the geographic and climatic variation among modeled sites, and the careful model and data development all contribute to the usefulness of the results.

Table 13. Predicted Alachlor Solution Concentrations (ppb)

Iowa River at Marengo - Case I

Year	Annual Mean Conc.	Peak Daily	Monthly Mean			
			May	June	July	Aug
1969	5.79	247.4	44.2	24.0	1.30	0.04
1970	0.43	30.88	4.69	0.72	0.20	0.02
1971	0.93	32.66	3.43	7.16	0.54	0.04
1972	1.82	122.93	0.65	20.85	0.24	0.02
1973	0.95	60.72	8.64	2.63	0.28	0.02
1974	5.08	276.76	39.91	20.05	0.85	0.02
1975	1.78	69.58	1.91	18.94	0.41	0.02
1976	1.67	77.17	7.75	11.96	0.25	0.02
1977	0.28	5.29	0.89	1.97	0.50	0.09
1978	3.49	202.33	21.09	16.38	4.49	0.02
10-year mean	2.24		13.32	12.46	0.91	0.04

Iowa River at Marengo - Case II

Year	Annual Mean Conc.	Peak Daily	Monthly Mean			
			May	June	July	Aug
1969	2.67	114.01	20.37	11.05	0.60	0.02
1970	0.22	14.23	2.16	0.33	0.09	0.01
1971	0.43	15.05	1.58	3.30	0.25	0.02
1972	0.84	56.65	0.30	9.61	0.11	0.01
1973	0.44	27.98	3.98	1.21	0.13	0.01
1974	2.34	127.54	18.39	9.24	0.39	0.01
1975	0.82	32.11	0.88	8.73	0.19	0.01
1976	0.77	35.56	3.57	5.51	0.12	0.01
1977	0.13	2.44	0.41	0.91	0.23	0.04
1978	1.61	93.24	9.72	7.55	2.07	0.01
10-year Mean	1.03		6.14	5.74	0.42	0.02

Iowa River at Marengo - Case III

Year	Annual Mean Conc.	Peak Daily	Monthly Mean			
			May	June	July	Aug
1969	15.11	645.30	115.29	62.54	6.26	0.11
1970	1.25	80.54	12.23	1.87	0.51	0.06
1971	2.43	85.18	8.94	18.68	1.42	0.11
1972	4.75	320.64	1.70	54.39	0.62	0.11
1973	2.49	158.37	22.53	6.85	0.74	0.11
1974	13.24	721.88	104.09	52.30	2.21	0.11
1975	4.64	181.74	4.98	49.41	1.08	0.11
1976	4.36	201.27	20.21	31.19	0.68	0.11
1977	0.74	13.81	2.32	5.15	1.30	0.23
1978	9.11	527.74	55.02	42.73	11.72	0.11
10-year Mean	5.83		34.75	32.49	2.38	0.11

Table 13. Predicted Alachlor Solution Concentrations (ppb)

Iowa River at Marshalltown - Case I

Year	Annual Mean Conc.	Peak Daily	Monthly Mean			
			May	June	July	Aug
1969	4.99	301.70	34.05	24.17	1.52	0.02
1970	0.24	7.73	1.37	1.19	0.17	0.02
1971	1.17	77.08	4.84	8.66	0.61	0.04
1972	1.39	133.80	0.87	15.45	0.24	0.02
1973	0.87	86.93	8.40	1.52	0.35	0.02
1974	4.45	321.68	33.27	19.42	0.69	0.02
1975	2.02	86.71	2.13	21.81	0.24	0.02
1976	1.39	99.62	8.92	7.44	0.20	0.02
1977	0.43	20.09	1.00	3.62	0.54	0.09
1978	2.47	87.82	8.51	17.77	3.52	0.02
10-year Mean	1.95		10.33	12.11	0.80	0.03

Iowa River at Marshalltown - Case II

Year	Annual Mean Conc.	Peak Daily	Monthly Mean			
			May	June	July	Aug
1969	2.30	139.03	15.69	11.14	0.70	0.01
1970	0.11	3.56	0.63	0.55	0.08	0.01
1971	0.54	34.52	2.23	3.99	0.28	0.02
1972	0.64	61.66	0.40	7.12	0.11	0.01
1973	0.40	40.06	3.87	0.70	0.16	0.01
1974	2.05	148.24	15.33	8.95	0.32	0.01
1975	0.93	39.96	0.98	10.05	0.11	0.01
1976	0.64	45.91	4.11	3.43	0.09	0.01
1977	0.20	9.26	0.46	1.67	0.25	0.04
1978	1.14	40.47	3.92	8.19	1.62	0.01
10-year Mean	0.90		4.76	5.58	0.37	0.01

Iowa River at Marshalltown - Case III

Year	Annual Mean Conc.	Peak Daily	Monthly Mean			
			May	June	July	Aug
1969	13.02	786.91	88.81	63.05	3.96	0.06
1970	0.62	20.15	3.57	3.11	0.45	0.06
1971	3.05	195.38	12.62	22.58	1.58	0.11
1972	3.62	349.00	2.26	40.30	0.62	0.06
1973	2.26	226.74	21.90	3.96	0.91	0.06
1974	11.60	839.04	86.77	50.66	1.81	0.06
1975	5.26	226.17	5.55	56.88	0.62	0.06
1976	3.62	259.85	23.26	19.41	0.51	0.06
1977	1.13	52.41	2.60	9.45	1.42	0.23
1978	6.45	229.06	22.19	43.36	9.17	0.06
10-year Mean	5.09		26.94	31.58	2.09	0.08

Table 13. Predicted Alachlor Solution Concentrations (ppb)

Iowa River at Rowan - Case I

Year	Annual Mean Conc.	Peak Daily	Monthly Mean			
			May	June	July	Aug
1969	2.19	120.61	11.22	13.48	1.19	0.02
1970	0.37	19.42	1.35	2.84	0.17	0.02
1971	0.69	30.58	4.04	3.12	1.04	0.17
1972	0.63	69.48	0.33	6.77	0.41	0.02
1973	0.24	12.80	1.26	1.39	0.30	0.02
1974	1.48	66.29	6.23	10.78	0.52	0.02
1975	1.54	81.98	2.76	15.54	0.11	0.02
1976	0.52	26.79	2.39	3.62	0.09	0.00
1977	0.89	58.13	1.61	7.29	1.37	0.39
1978	1.32	74.24	5.73	9.27	0.78	0.02
10-year Mean	0.98		3.69	7.42	0.61	0.07

Iowa River at Rowan - Case II

Year	Annual Mean Conc.	Peak Daily	Monthly Mean			
			May	June	July	Aug
1969	1.00	55.58	5.17	6.21	0.55	0.01
1970	0.17	8.95	0.62	1.31	0.08	0.01
1971	0.32	14.09	1.86	1.44	0.48	0.08
1972	0.29	32.02	0.15	3.12	0.19	0.01
1973	0.11	5.90	0.58	0.64	0.14	0.01
1974	0.68	30.55	2.87	4.97	0.24	0.01
1975	0.71	37.78	1.27	7.16	0.05	0.01
1976	0.24	12.18	1.10	1.67	0.04	0.00
1977	0.41	26.79	0.74	3.36	0.63	0.18
1978	0.61	34.21	2.64	4.27	0.36	0.01
10-year Mean	0.45		1.70	3.42	0.28	0.03

Iowa River at Rowan - Case III

Year	Annual Mean Conc.	Peak Daily	Monthly Mean			
			May	June	July	Aug
1969	5.66	314.58	29.26	35.15	3.11	0.06
1970	0.96	50.66	3.51	7.41	0.45	0.06
1971	1.81	79.75	10.53	8.15	2.72	0.45
1972	1.64	181.23	0.85	17.66	1.08	0.06
1973	0.62	33.39	3.28	3.62	0.79	0.06
1974	3.85	172.91	16.24	28.13	1.36	0.06
1975	4.02	213.83	7.19	40.53	0.28	0.06
1976	1.36	68.94	6.23	9.46	0.23	0.00
1977	2.32	151.63	4.19	19.02	3.57	1.02
1978	6.27	193.63	14.94	24.17	2.04	0.06
10-year Mean	2.55		9.62	19.36	1.58	0.19

Table 14. Predicted Alachlor Solution Concentrations (ppb)

	10-Year Mean	Peak Daily	Monthly Means May	June	July	Aug.
Yazoo River, MS - Case II						
Yazoo R. at Lambert	0.18	23.45	0.04	1.98	0.11	0.01
Yazoo R. at Swan Lake	0.13	21.14	0.03	1.48	0.05	0.01
Yazoo River, MS - Case III						
Yazoo R. at Lambert	1.25	162.74	0.28	13.74	0.76	0.07
Yazoo R. at Swan Lake	0.90	146.71	0.21	10.27	0.35	0.07

Table 15. Predicted Alachlor Concentrations (ppb)

	10-Year Mean	Peak Daily	Monthly Means Feb	Mar	Apr	May	June
Little River, GA - Case II							
Little R. GA.	0.12	14.50	0.00	1.08	0.28	0.04	0.01
Little River, GA - Case III							
Little R. GA.	0.56	67.86	0.01	5.05	1.31	0.19	0.05

2. Applicator Exposure

Alachlor is applied once per growing season prior to or immediately after planting. Three groups of applicators are exposed to alachlor. These are the private farmer, the custom applicator and the aerial applicator. Approximately 70% of the alachlor applied per year is applied by the private farmer. Less than 1% was applied aerially; however, aerial application of alachlor was voluntarily cancelled by Monsanto.

The registrant has submitted studies which measured worker exposure to alachlor during aerial and ground applications of the emulsifiable concentrate, microencapsulated and granular formulations (Lauer and Arras, 1981). The inhalation and dermal exposures to the mixer/loader, pilot and flagger were measured during aerial application and the exposure of the mixer/loader and applicator was measured during ground application. Dermal exposure was assessed by measuring residue deposits on gloves or gauze pads and respiratory exposure was assessed through the extraction of foam plugs, silica gel and charcoal from air samples taken near the breathing zone.

The exposure situation which the Agency considers to be appropriate for analysis of occupational exposure to alachlor assumes the worker is wearing protective clothing such as coveralls and rubber gloves (during mixing and loading). Protection of this type is assumed to reduce exposure to covered body areas by about 80% because some pesticide will penetrate the material or filter in around edges and hems. Accordingly, the exposure assessment presented in Table 16 uses the Monsanto data conducted with protected workers and adjusts for exposure to body areas based on this 80% figure. Inhalation exposure is insignificant compared to dermal exposure. For example, the exposure figures for a mixer/loader (ground tank fill) assuming 80% protection are .44 mg/kg/day for dermal and .00027 mg/kg/day for inhalation. This range in exposure figures is consistent for each use pattern. The following three tables, Tables 16, 17 and 18, present exposure estimates resulting from the use of different assumptions regarding protective clothing. In Table 17, the worker is unprotected. In Table 18, the face, back of the neck, front of the neck and "v" of the chest are exposed, rubber gloves are worn and the rest of the body is completely protected.

Current occupational exposure to alachlor probably does not reflect the protections outlined in the two more restrictive exposure situations discussed above. Therefore, the occupational exposure estimates presented in Tables 16 and 18 may underestimate actual current exposure. However, the protective measures assumed in Table 16 could be readily and easily required and reasonable compliance with such requirements seems likely. These are the requirements to be implemented prior to the 1985 season under the alachlor Registration Standard.

The Agency believes that the exposure estimates presented in Table 16 are the most relevant for risk assessment purposes. The Agency also believes that most pilots do not mix/load pesticides prior to aerial application. Exposure estimates for pilots and mixer/loaders have therefore not been combined. The mixer/loader and aerial applicator exposure estimates should be considered separately. For ground application, the mixer/loader and ground applicator are usually not the same individual and those exposure estimates should also be considered separately.

In assessing applicator exposure for oncogenic risk assessment purposes, it is assumed that an individual is exposed for a 40 year working lifetime during a 70 year lifespan. The exposure estimate also adjusts for the estimated number of days per year that an applicator is exposed (1 to 6 days for a private farmer, 5 to 30 days for a custom ground applicator and 5 to 10 days for an aerial applicator of alachlor) and present the range in applicator exposure expected from applying a alachlor at 2 lbs/acre to 4 lbs/acre . The exposure (received over a 40 year working life) is therefore an average of the exposure level on the exposed days and the unexposed days over a 70 year lifetime.

The following tables present applicator exposure estimates for the three degrees of protective clothing discussed previously. The latter two columns in these tables reflect the range of exposure taking into account the likely number of days per year that exposure may occur. All figures assume a 50% dermal absorption rate with the exception of the microencapsulated formulation where 12% absorption is assumed. These figures are based on dermal absorption studies submitted by Monsanto using human skin and in vivo studies using Rhesus monkeys (Monsanto, 1981a & 1981b).

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Table 16. Alachlor Worker Exposure (mg/kg/day) with Protection (80%)*

Use Pattern	Exposure on Day of Application	Lifetime Average Exposure By Days of Exposure/Year	
		1 day/year	30 days/year
		LASSO EC	
Ground Tank Fill	2×10^{-1}	4×10^{-4}	1×10^{-2}
Ground Applicator	2×10^{-2}	3×10^{-5}	1×10^{-3}
Ground Transfer (Closed System)			
5 gal container	2×10^{-2}	3×10^{-5}	8×10^{-4}
55 gal container	1×10^{-1}	2×10^{-4}	5×10^{-3}
Aerial Application**		5 d/year	10 d/year
Tank Fill	2×10^{-0}	2×10^{-2}	3×10^{-2}
Pilot	1×10^{-1}	9×10^{-4}	2×10^{-3}
Flagger	4×10^{-1}	3×10^{-3}	5×10^{-2}
	Other Formulations of LASSO		
Micro-Encapsulated		1 d/year	30 d/year
Mixer-Loader	8×10^{-2}	1×10^{-4}	4×10^{-3}
Applicator	9×10^{-3}	1×10^{-5}	4×10^{-4}
Combined	9×10^{-2}	1×10^{-4}	4×10^{-3}
Granular (LASSO II)			
Mixer-Loader	1×10^{-1}	8×10^{-4}	2×10^{-2}
Applicator	3×10^{-4}	2×10^{-6}	6×10^{-5}
Combined	1×10^{-1}	8×10^{-4}	2×10^{-2}

* Exposure estimates assume an application rate of 4 lbs per acre. Estimated exposure from other rates will be proportional to the application rate.

**Aerial application has been discontinued.

Table 17. Alachlor Worker Exposure (mg/kg/day)
No Protection*

Use Pattern	Exposure on Day of Application	Lifetime Average Exposure By Days of Exposure/Year	
		1 day/year	30 days/year
		LASSO EC	
Ground Tank Fill	1.9×10^0	3×10^{-3}	9×10^{-2}
Ground Applicator	7×10^{-2}	1×10^{-4}	3×10^{-3}
Ground Transfer (Closed System)			
5 gal container	1×10^0	2×10^{-3}	6×10^{-2}
55 gal container	9×10^{-1}	8×10^{-4}	4×10^{-2}
Aerial Application**		5 d/year	10 d/year
Tank Fill	9×10^0	7×10^{-2}	2×10^{-1}
Pilot	4×10^{-1}	4×10^{-3}	7×10^{-3}
Flagger	1×10^1	1×10^{-1}	2×10^{-1}
	Other Formulations of LASSO		
Micro-Encapsulated		1 d/year	30 d/year
Mixer-Loader	1×10^{-1}	2×10^{-4}	7×10^{-3}
Applicator	9×10^{-3}	1×10^{-5}	4×10^{-4}
Combined	1×10^{-1}	1×10^{-4}	4×10^{-3}
Granular (LASSO II)			
Mixer-Loader	2×10^0	4×10^{-3}	1×10^{-1}
Applicator	4×10^{-3}	6×10^{-6}	2×10^{-4}
Combined	2×10^0	4×10^{-3}	1×10^{-1}

* Exposure estimates assume an application rate of 4 lbs per acre. Estimated exposure from other rates will be proportional to the application rate.

** Aerial application has been discontinued.

Table 18. Alachlor Worker Exposure (mg/kg/day)
With 100% Protection*

Use Pattern	Exposure on Day of Application	Lifetime Average Exposure By Days of Exposure/Year	
		1 day/year	30 days/year
		LASSO EC	
Ground Tank Fill	5×10^{-2}	8×10^{-5}	1×10^{-3}
Ground Applicator	1×10^{-2}	2×10^{-5}	5×10^{-4}
Ground Transfer (Closed System)			
5 gal container	1×10^{-2}	2×10^{-2}	6×10^{-4}
55 gal container	3×10^{-2}	5×10^{-5}	1×10^{-3}
Aerial Application**			
Tank Fill	1×10^{-1}	9×10^{-4}	2×10^{-3}
Pilot	3×10^{-2}	2×10^{-4}	5×10^{-4}
Flagger	1×10^{0}	9×10^{-3}	2×10^{-2}
	Other Formulations of LASSO		
Micro-Encapsulated			
Mixer-Loader	7×10^{-2}	1×10^{-4}	3×10^{-3}
Applicator	8×10^{-3}	1×10^{-5}	4×10^{-4}
Combined	8×10^{-2}	1×10^{-4}	3×10^{-3}
Granular (LASSO II)			
Mixer-Loader	5×10^{-3}	4×10^{-6}	2×10^{-4}
Applicator	7×10^{-4}	6×10^{-7}	2×10^{-5}
Combined	1×10^{-2}	1×10^{-5}	2×10^{-4}

* Exposure estimates assume an application rate of 4 lbs per acre. Estimated exposure from other rates will be proportional to the application rate.

** Aerial application has been discontinued.

The Agency has determined that a substantial number of workers are exposed to alachlor during application operations. Most of these workers are exposed during application at rates of 2 lb/acre or less. For example, for field corn only about 22% of the applicators are exposed to more than 2 lb/acre. Estimates of the number of individuals in each occupational exposure group are presented in Table 19. The approximately 650,000 private farmers who apply alachlor using ground equipment and the 650,000 mixer/loaders associated with the same operation can be exposed to alachlor from 1 to 6 days per year. The approximately 89,000 custom applicators, and associated mixer/loaders, using ground equipment can be exposed to alachlor from 5 to 30 days per year. There was limited use of aerial application, therefore, only about 1000 aerial applicators, 1000 aerial mixer/loaders and 100 flaggers were exposed for 5 to 10 days per year.

Table 19. Estimated Number of Applicators, Mixer-Loaders and Flaggers Potentially Exposed to Alachlor Herbicide Per Year

Site	Custom Ground Applicators	Private Farmer Ground Applicators	Aerial Custom Applicators	Private Farmer Ground Mixer/Loaders	Custom Ground and Aerial Mixer/Loaders	Flaggers (Assuming 10% human, 90% automatic)
Soybeans	1,500	408,900	—	408,900	1,500	—
Peanuts	480	15,500	160	15,500	750	20
Corn	87,000	215,000	880	215,000	87,800	88
Green Peas		210		210		
Lima Beans, Dry Beans, Kidney Beans, Mung Beans		2,300		2,300		
Cotton		150		150		
Sunflowers		360		360		
Grain Sorghum		4,300		4,300		
Potatoes		4,700		4,700		
TOTALS	88,980	651,420	1,040	651,420	90,050	108

D. Risk Characterization

The plausible upper limit to the excess cancer risk is obtained by taking the Q_1*s from the Dose-Response Assessment (5×10^{-2} to 1×10^{-1} per mg/kg/day) and multiplying it by the estimates from the Exposure Assessment. The result is coupled with estimates of the certainty/uncertainty in the Hazard Identification and Exposure Assessment to provide a final conclusion. As previously noted, the Agency has assigned alachlor to category B2 (a probable human carcinogen) of the EPA modification of the IARC classification scheme. The risk estimates in this document should be interpreted in the context of this classification.

1. Dietary Risks

a. Risks from Consumption of Raw Agricultural Commodities

Exposure estimates and corresponding risks are presented in Table 20. As explained in Section II.B., maximum exposure estimates were developed from tolerances established for residues of alachlor in foods. It is assumed that residues are present in all individual raw agricultural commodities to the extent permitted by the tolerances, e.g. all corn consumed by an individual has a residue of 0.2 ppm alachlor. It is also assumed that the total daily diet is 1.5 kg and that the average body weight is 60 kg. The best estimates were developed based on available information on residue levels actually measured in field tests. All exposures in Table 20 were developed using the EPA food factor system.

Both the TMRC and best estimates, however, may underestimate exposures to residues of concern because of limitations mentioned above in the analytical method to detect metabolic products of alachlor. Note that estimates presented here for total dietary exposure and risk do not consider exposure through drinking water.

Table 20. Quantitative Assessment of Dietary Risks for Alachlor

Crop	Theoretical Maximum Residue Contribution		Best Available Estimate*	
	Dietary Exposure (mg/kg/d)	Upper 95% Bound on Risk	Dietary Exposure (mg/kg/d)	Upper 95% Bound on Risk
corn	1×10^{-4}	$10^{-6} - 10^{-5}$	3×10^{-5}	$10^{-7} - 10^{-6}$
soybeans	5×10^{-5}	$10^{-6} - 10^{-5}$	2×10^{-5}	10^{-6}
Beans, dry edible	8×10^{-6}	$10^{-7} - 10^{-6}$	7×10^{-6}	$10^{-7} - 10^{-6}$
beans, Lima	5×10^{-6}	$10^{-7} - 10^{-6}$	4×10^{-6}	$10^{-7} - 10^{-6}$
Peas	2×10^{-5}	10^{-6}	2×10^{-5}	10^{-6}
**Potatoes	1×10^{-4}	$10^{-6} - 10^{-5}$	1×10^{-4}	$10^{-6} - 10^{-5}$
Cottonseed (oil)	2×10^{-6}	10^{-7}	7×10^{-7}	$10^{-8} - 10^{-7}$
Peanuts	5×10^{-6}	$10^{-7} - 10^{-6}$	2×10^{-6}	10^{-7}
Sorghum	8×10^{-7}	$10^{-8} - 10^{-7}$	4×10^{-7}	$10^{-8} - 10^{-7}$
Sunflower	2×10^{-6}	10^{-7}	2×10^{-6}	10^{-7}
Milk & Dairy	1×10^{-4}	$10^{-6} - 10^{-5}$	1×10^{-4}	$10^{-6} - 10^{-5}$
Meat & Poultry	7×10^{-5}	$10^{-6} - 10^{-5}$	7×10^{-5}	$10^{-6} - 10^{-5}$
Eggs	1×10^{-6}	$10^{-8} - 10^{-7}$	1×10^{-6}	$10^{-8} - 10^{-7}$
TOTAL	6×10^{-4}	$10^{-5} - 10^{-4}$	4×10^{-4}	$10^{-5} - 10^{-4}$

*Limit of reliable quantification = 0.05 - 0.1 ppm.

**The potato use has been discontinued. Removal of the contribution from potatoes would reduce the total TMRC to 5×10^{-4} mg/kg/day and the total Best Available Estimate to 3×10^{-4} mg/kg/day. The estimated upper 95% bound on risk would remain in the $10^{-5} - 10^{-4}$ range in both cases.

Table 21 contains the exposure and associated upper bound risk estimates derived from use of the Agency's new Tolerance Assessment System as discussed in Chapter II.C.l.a. As noted earlier, the TAS exposure estimates, in general, are similar to those obtained from the Agency's traditional approach. Children and infants estimates are different because their diet is so different from adults. These diets, of course, are not lifetime exposures and, therefore, need to interpreted with care. The children's and infant diets would yield the appropriate exposure estimate if risk is in fact determined by the level of exposure early in life or by the highest exposure occurring for any short portion of the lifespan. It would overstate exposure if the average exposure over a lifetime is the determining factor for health effects. There is no way to differentiate between these possibilities in the animal studies, which have a relatively constant exposure over the animal's entire lifetime. The chronic rat study extension, which exposed animals to dose levels of 126 mg/kg/day either for a lifetime or for a quarter of a lifetime, suggested that early exposure to young animals may contribute disportionately to the induction of nasal turbinate tumors. However, this extension of the chronic study was not designed to investigate the effect of early exposure to alachlor on induction of tumors. The potential bias in the selection of animals removed from exposure to alachlor limit the conclusions that can be drawn regarding the effect of partial lifetime exposure on tumor induction.

Table 21. Estimated Dietary Exposure (mg/kg/day) to Alachlor from Treated Crops and Corresponding Upper Limits of Excess Cancer Risks for Population Subgroups[1/]

Population Subgroup	Estimated Dietary Exposure	Corresponding Upper Limit of Excess Cancer Risk Estimate
Population: 48 states (All Seasons)	5×10^{-4}	$10^{-5} - 10^{-4}$
Spring	4×10^{-4}	$10^{-5} - 10^{-4}$
Summer	5×10^{-4}	$10^{-5} - 10^{-4}$
Fall	5×10^{-4}	$10^{-5} - 10^{-4}$
Winter	5×10^{-4}	$10^{-5} - 10^{-4}$
Northeast Region	4×10^{-4}	$10^{-5} - 10^{-4}$
North Central Region	5×10^{-4}	$10^{-5} - 10^{-4}$
Southern Region	4×10^{-4}	$10^{-5} - 10^{-4}$
Western Region	5×10^{-4}	$10^{-5} - 10^{-4}$
Hispanic	6×10^{-4}	$10^{-5} - 10^{-4}$
Non-Hispanic Whites	5×10^{-4}	$10^{-5} - 10^{-4}$
Non-Hispanic Blacks	5×10^{-4}	$10^{-5} - 10^{-4}$
Non-Hispanic Other	5×10^{-4}	$10^{-5} - 10^{-4}$
Nursing Infants (less than 1 year)	4×10^{-4}	$10^{-5} - 10^{-4}$
Non-Nursing Infants (less than 1 year)	2×10^{-3}	10^{-4}
Female (13 years or more, Pregnant)	3×10^{-4}	$10^{-5} - 10^{-4}$
Female (13 years or more, Nursing)	4×10^{-4}	$10^{-5} - 10^{-4}$
Children (1-6 years)	1×10^{-3}	$10^{-5} - 10^{-4}$
Children (7-12 years)	7×10^{-4}	$10^{-5} - 10^{-4}$
Male 13-19 years	5×10^{-4}	$10^{-5} - 10^{-4}$
Female 13-19 years (not pregnant or nursing)	4×10^{-4}	$10^{-5} - 10^{-4}$
Males (20 years or more)	3×10^{-4}	$10^{-5} - 10^{-4}$
Females (20 years of more not pregnant or nursing)	3×10^{-4}	$10^{-5} - 10^{-4}$

[1/] See text for explanatory note on infant and child risk estimation.

b. Drinking Water Risks

As discussed in Chapter II.C.1.b., there is also a potential for exposure to alachlor in drinking water. A time weighted average of 2 to 5 ppb was determined to be a realistic estimate of exposure from alachlor contaminated surface water for the cornbelt area. Assuming that a 10 kg child consumes one liter of water per day and that water contains 2 ppb alachlor, the alachlor exposure would be 2 micrograms/kg body-weight/day. If it is further assumed that this is for a lifetime of exposure, a level of 2 ppb would be associated with an upper 95% bound estimate of lifetime cancer risk of approximately 10^{-5}. A time weighted average of 5 ppb, using the same assumptions, would result in a range of upper bound risk estimates of 10^{-4} to 10^{-5}.

The previously discussed surface water modeling indicates that occasional yearly averages of 15 ppb may be expected in areas of substantial alachlor use such as in portions of the corn belt and that occasional levels much higher than this may be expected on certain days. However, the significance of these temporarily higher levels for cancer risk assessment is unknown. Some of the uncertainties of risks associated with partial lifetime exposure were discussed in Chapter II.D.1.a.

Use of available averages of samples where contamination was found, rather than modeling estimates, would result in similar risk estimates. Table 22 presents the upper 95% bound on estimated lifetime cancer risk for various levels of alachlor in drinking water. Risk estimates are presented for both the 10 kg child drinking 1 liter of water per day and the 60 kg adult drinking two liters of water per day. Although a lifetime of exposure is assumed in each case, the available data do not allow the determination of which individual (the 10 Kg child or the 60 kg adult) is a more appropriate model. The range of potential risks indicated by the two models should be considered. The risk estimates are conservative and subject to over estimation of risk and tend to stress the Agency's concern over early exposure.

Table 22. Assessment of Drinking Water Risks for Alachlor*

Exposure Level (ppb)	Upper Limit Estimate of Lifetime Cancer Risk	
	10 Kg Child	60 Kg Adult
0.15	10^{-6}	10^{-7} to 10^{-6}
1.5	10^{-5}	10^{-6} to 10^{-5}
15.0	10^{-4}	10^{-5} to 10^{-4}

* See page 53 for explanatory note on infant and child risk estimation.

Table 24. Alachlor Worker Upper Limit Risk Estimates
No Protection

Product	Use Pattern	Days/year	Lifetime Exposure* mg/kg/day	Upper 95% on Risk
LASSO EC	Ground Tank Fill	1 d/y	$2 \times 10^{-3} - 3 \times 10^{-3}$	$10^{-4} - 10^{-}$
		30 d/y	$5 \times 10^{-2} - 9 \times 10^{-2}$	$10^{-3} - 10^{-}$
	Ground Applicator	1 d/y	$5 \times 10^{-5} - 1 \times 10^{-4}$	$10^{-6} - 10^{-}$
		30 d/y	$2 \times 10^{-3} - 3 \times 10^{-3}$	$10^{-4} - 10^{-}$
	Ground Transfer (Closed System) 5 gal container	1 d/y	$1 \times 10^{-3} - 2 \times 10^{-3}$	$10^{-5} - 10^{-4}$
		30 d/y	$2 \times 10^{-2} - 6 \times 10$	$10^{-3} - 10^{-2}$
	Ground Transfer (Closed System) 55 gal container	1 d/y	$1 \times 10^{-3} - 2 \times 10^{-3}$	$10^{-5} - 10^{-4}$
		30 d/y	$1 \times 10^{-2} - 2 \times 10^{-}$	$10^{-4} - 10^{-3}$
	Aerial** Application: Tank Fill	5 d/y	$4 \times 10^{-2} - 7 \times 10^{-2}$	$10^{-3} - 10^{-2}$
		10 d/y	$1 \times 10^{-1} - 2 \times 10^{0}$;	$10^{-3} - 10^{-2}$
	Aerial** Application: Pilot	5 d/y	$2 \times 10^{-3} - 4 \times 10^{-3}$	$10^{-4} - 10^{-3}$
		10 d/y	$4 \times 10^{-3} - 7 \times 10^{-3}$	$10^{-4} - 10^{-3}$
	Aerial** Application: Flagger	5 d/y	$5 \times 10^{-2} - 1 \times 10^{-1}$	$10^{-3} - 10^{-2}$
		10 d/y	$1 \times 10^{-1} - 2 \times 10^{-1}$	$10^{-3} - 10^{-2}$
Micro Encapsulated	Mixer Loader	1 d/y	$1 \times 10^{-4} - 2 \times 10^{-4}$	$10^{-6} - 10^{-5}$
		30 d/y	$4 \times 10^{-3} - 7 \times 10^{-3}$	$10^{-4} - 10^{-3}$
	Applicator	1 d/y	$5 \times 10^{-6} - 1 \times 10^{-5}$	$10^{-7} - 10^{-6}$
		30 d/y	$4 \times 10^{-4} - 4 \times 10^{-4}$	$10^{-5} - 10^{-4}$
	Combined	1 d/y	$5 \times 10^{-5} - 1 \times 10^{-4}$	$10^{-6} - 10^{-5}$
		30 d/y	$2 \times 10^{-3} - 4 \times 10^{-3}$	$10^{-4} - 10^{-3}$
Granular (LASSO II)	Mixer Loader	1 d/y	$2 \times 10^{-3} - 4 \times 10^{-3}$	$10^{-4} - 10^{-3}$
		30 d/y	$5 \times 10^{-2} - 1 \times 10^{-1}$	$10^{-3} - 10^{-2}$
	Applicator	1 d/y	$3 \times 10^{-6} - 6 \times 10^{-6}$	$10^{-7} - 10^{-6}$
		30 d/y	$2 \times 10^{-4} - 2 \times 10^{-4}$	$10^{-6} - 10^{-5}$
	Combined	1 d/y	$2 \times 10^{-3} - 4 \times 10^{-3}$	$10^{-4} - 10^{-3}$
		30 d/y	$1 \times 10^{-4} - 1 \times 10^{-1}$	$10^{-3} - 10^{-2}$

* Range represents estimated exposures from applying alachlor at from 2 lbs/acre to 4 lbs/acre rates.

** Aerial application is being discontinued.

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Table 23. Alachlor Worker Upper Limit Risk Estimates
80% Protection

Product	Use Pattern	Days/year	Lifetime Exposure* mg/kg/day	Upper 95% Bound on Risk
LASSO EC	Ground Tank Fill	1 d/y	$2 \times 10^{-4} - 4 \times 10^{-4}$	$10^{-5} - 10^{-4}$
		30 d/y	$5 \times 10^{-3} - 1 \times 10^{-2}$	$10^{-4} - 10^{-3}$
	Ground Applicator	1 d/y	$2 \times 10^{-5} - 3 \times 10^{-3}$	$10^{-6} - 10^{-5}$
		30 d/y	$5 \times 10^{-4} - 1 \times 10^{-3}$	$10^{-5} - 10^{-4}$
	Ground Transfer (Closed System) 5 gal container	1 d/y	$2 \times 10^{-5} - 3 \times 10^{-5}$	$10^{-6} - 10^{-5}$
		30 d/y	$4 \times 10^{-4} - 8 \times 10^{-4}$	$10^{-5} - 10^{-4}$
	Ground Transfer (Closed System) 55 gal container	1 d/y	$1 \times 10^{-4} - 2 \times 10^{-4}$	$10^{-6} - 10^{-5}$
		30 d/y	$3 \times 10^{-3} - 5 \times 10^{-3}$	$10^{-4} - 10^{-3}$
	Aerial** Application: Tank Fill	5 d/y	$1 \times 10^{-2} - 2 \times 10^{-2}$	$10^{-4} - 10^{-3}$
		10 d/y	$2 \times 10^{-2} - 3 \times 10^{-2}$	$10^{-3} - 10^{-2}$
	Aerial** Application: Pilot	5 d/y	$5 \times 10^{-4} - 9 \times 10^{-4}$	$10^{-5} - 10^{-4}$
		10 d/y	$1 \times 10^{-3} - 2 \times 10^{-3}$	$10^{-5} - 10^{-4}$
	Aerial** Application: Flagger	5 d/y	$2 \times 10^{-2} - 3 \times 10^{-2}$	$10^{-3} - 10^{-2}$
		10 d/y	$3 \times 10^{-2} - 5 \times 10^{-2}$	$10^{-3} - 10^{-2}$
Micro Encapsulated	Mixer Loader	1 d/y	$5 \times 10^{-2} - 1 \times 10^{-4}$	$10^{-6} - 10^{-5}$
		30 d/y	$2 \times 10^{-3} - 4 \times 10^{-3}$	$10^{-4} - 10^{-3}$
	Applicator	1 d/y	$5 \times 10^{-6} - 1 \times 10^{-5}$	$10^{-7} - 10^{-6}$
		30 d/y	$2 \times 10^{-4} - 4 \times 10^{-4}$	$10^{-5} - 10^{-4}$
	Combined	1 d/y	$5 \times 10^{-5} - 1 \times 10^{-4}$	$10^{-6} - 10^{-5}$
		30 d/y	$2 \times 10^{-3} - 4 \times 10^{-3}$	$10^{-4} - 10^{-3}$
Granular (LASSO II)	Mixer Loader	1 d/y	$4 \times 10^{-4} - 8 \times 10^{-4}$	$10^{-5} - 10^{-4}$
		30 d/y	$1 \times 10^{-2} - 2 \times 10^{-2}$	$10^{-4} - 10^{-3}$
	Applicator	1 d/y	$1 \times 10^{-6} - 2 \times 10^{-6}$	$10^{-8} - 10^{-7}$
		30 d/y	$3 \times 10^{-5} - 6 \times 10^{-5}$	$10^{-6} - 10^{-5}$
	Combined	1 d/y	$4 \times 10^{-4} - 8 \times 10^{-4}$	$10^{-5} - 10^{-4}$
		30 d/y	$1 \times 10^{-2} - 2 \times 10^{-2}$	$10^{-4} - 10^{-3}$

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* Range represents estimated exposure from applying alachlor at 2 lbs/acre to 4 lbs/acre rates.

** Aerial application is being discontinued.

2. Applicator Risks

Estimated applicator cancer risks in Table 23 are for the exposure situation considered most relevant to actual application conditions. That situation assumes that the worker is wearing protective clothing such as coveralls and rubber gloves during mixing and loading. Rubber gloves are generally not worn during application. Protective clothing in this case reduces exposure to covered body areas by 80% from the case of a worker who is virtually unprotected. A 50% dermal exposure is assumed for all exposures except for the microencapsulated product for which a 12% dermal absorption is assumed (Monsanto, 1981a & 1981b). The risk estimates presented in Tables 24 and 25 are for the exposure situations which the Agency considers less likely to be applicable to actual applicator exposure. They are presented to illustrate the effect of various degrees of protective clothing on risk.

The estimates of cancer risk to occupationally exposed persons do not contain any component of dietary or drinking water exposure. Therefore, the appropriate estimates of cancer risk to workers using alachlor would be higher than these estimates because of the dietary exposure routes.

Table 25. Alachlor Worker Upper Limit Risk Estimates
100% Protection

Product	Use Pattern	Days/year	Lifetime Exposure* mg/kg/day	Upper 95% Bo on Risk
LASSO EC	Ground Tank Fill	1 d/y	$4 \times 10^{-5} - 8 \times 10^{-5}$	$10^{-6} - 10^{-5}$
		30 d/y	$5 \times 10^{-4} - 1 \times 10^{-3}$	$10^{-5} - 10^{-4}$
	Ground Applicator	1 d/y	$1 \times 10^{-5} - 2 \times 10^{-5}$	$10^{-7} - 10^{-6}$
		30 d/y	$3 \times 10^{-4} - 5 \times 10^{-4}$	$10^{-5} - 10^{-4}$
	Ground Transfer (Closed System) 5 gal container	1 d/y	$1 \times 10^{-5} - 2 \times 10^{-5}$	$10^{-7} - 10^{-6}$
		30 d/y	$3 \times 10^{-4} - 6 \times 10^{-4}$	$10^{-5} - 10^{-4}$
	Ground Transfer (Closed System) 55 gal container	1 d/y	$3 \times 10^{-5} - 5 \times 10^{-5}$	$10^{-6} - 10^{-5}$
		30 d/y	$5 \times 10^{-4} - 1 \times 10^{-3}$	$10^{-5} - 10^{-4}$
	Aerial** Application: Tank Fill	5 d/y	$5 \times 10^{-4} - 9 \times 10^{-4}$	$10^{-5} - 10^{-4}$
		10 d/y	$1 \times 10^{-3} - 2 \times 10^{-3}$	$10^{-5} - 10^{-4}$
	Aerial** Application: Pilot	5 d/y	$1 \times 10^{-4} - 2 \times 10^{-4}$	$10^{-6} - 10^{-5}$
		10 d/y	$3 \times 10^{-4} - 5 \times 10^{-4}$	$10^{-5} - 10^{-4}$
	Aerial** Application: Flagger	5 d/y	$5 \times 10^{-3} - 9 \times 10^{-3}$	$10^{-4} - 10^{-3}$
		10 d/y	$1 \times 10^{-2} - 2 \times 10^{-2}$	$10^{-4} - 10^{-3}$
Micro Encapsulated	Mixer Loader	1 d/y	$5 \times 10^{-5} - 1 \times 10^{-4}$	$10^{-6} - 10^{-5}$
		30 d/y	$2 \times 10^{-3} - 3 \times 10^{-3}$	$10^{-4} - 10^{-3}$
	Applicator	1 d/y	$5 \times 10^{-6} - 1 \times 10^{-5}$	$10^{-7} - 10^{-6}$
		30 d/y	$2 \times 10^{-4} - 4 \times 10^{-4}$	$10^{-5} - 10^{-4}$
	Combined	1 d/y	$5 \times 10^{-5} - 1 \times 10^{-4}$	$10^{-6} - 10^{-5}$
		30 d/y	$2 \times 10^{-3} - 4 \times 10^{-3}$	$10^{-4} - 10^{-3}$
Granular (LASSO II)	Mixer Loader	1 d/y	$2 \times 10^{-6} - 4 \times 10^{-6}$	$10^{-7} - 10^{-6}$
		30 d/y	$1 \times 10^{-4} - 2 \times 10^{-4}$	$10^{-6} - 10^{-5}$
	Applicator	1 d/y	$3 \times 10^{-7} - 6 \times 10^{-7}$	$10^{-8} - 10^{-7}$
		30 d/y	$1 \times 10^{-5} - 2 \times 10^{-3}$	$10^{-7} - 10^{-6}$
	Combined	1 d/y	$5 \times 10^{-6} - 1 \times 10^{-5}$	$10^{-7} - 10^{-6}$
		30 d/y	$1 \times 10^{-4} - 2 \times 10^{-4}$	$10^{-6} - 10^{-5}$

* Range represents estimated exposures from applying alachlor at from 2 lbs/acre to 4 lbs/acre rates.

** Aerial application is being discontinued.

3. Uncertainties in the Risk Assessment

The risk assessment approach contains a number of uncertainties, the sources of which have been discussed above.

The quantitative risk estimates contain a great deal of uncertainty because they must necessarily extrapolate from laboratory animals to humans and from the very high exposures used in the laboratory studies to the generally much lower and less well characterized human exposures. The Agency's approach has been to present plausible upper bounds to the risk as a rough indication of what potential risks might be.

Dietary exposure estimates are a source of uncertainties, some of which have been discussed in Chapter II.C.1.a. Estimates of residues in meat, milk, poultry and eggs are hampered by the lack of adequate residue data. The levels of the parent compound and the metabolites containing the diethylaniline moiety may be less than the tolerances set at the sensitivity of the analytical method (0.02 ppm) and the use of 0.02 ppm as a residue estimate, therefore, may tend to overestimate the exposure and risk associated with the parent compound.

On the other hand, insufficient data are available on the metabolism of alachlor in domestic animals and the transfer of alachlor residues from treated feeds to animal tissues and milk. It may be that there are metabolites of toxicological concern which are not being measured by the available analytical method used to determine compliance with the tolerances. The total residue of concern, therefore, may turn out to be higher than the currently permitted maximum level. Additional metabolism data are being required as a basis to maintain alachlor registrations even during the period of administrative review of this chemical. In order to avoid suspension of the registration under FIFRA §3(c)(2)(B) data "call-in" provisions, the registrant must submit such data in the near future (see Registration Standard for alachlor).

Similarly, there are indications that the present enforcement method associated with the soybean tolerances does not measure the entire residue of concern on this crop. The level of the total residue of concern may, therefore, be higher than indicated here. Additional data are also being requested on this issue.

Variation in individual food intake patterns is another source of uncertainty in estimating health risks from dietary exposure to alachlor. The dietary burdens in the dietary risk table (Table 20) were based upon standard food factors used by the Agency for many years to represent typical diets. Although these standard food factors are appropriate for estimating average population risk, some individuals and subgroups within the population will be at greater (or lesser) risk because their diets contain more (or less) of the food with alachlor residues.

Some of the uncertainties of risks associated with partial lifetime exposures were discussed in Chapter II.D.l.a.

Finally, none of these dietary exposure estimates include the contribution of contaminated drinking water to total dietary intake of alachlor. The extent of drinking water contamination by alachlor is itself an uncertainty and the limitations of the available monitoring data have been previously discussed.

Uncertainties also exist in the area of applicator exposure and risk, and the primary uncertainty in this area relates to dermal absorption. The previously submitted dermal absorption studies suggest rates of 50% for all formulations other than the microencapsulated product for which a rate of 12% is suggested. However, the available studies have serious deficiencies in study methodology which have led to the requesting of additional information regarding the dermal absorption of all three formulations.

E. Toxicity of Alternatives to Alachlor

Table 26 summarizes the use patterns for the most likely alternatives to alachlor. Based on the current and projected use patterns of these compounds the primary alternative appears to be metolachlor.

Metolachlor has a fairly complete toxicology data base, lacking only mutagenicity studies, and a Registration Standard was issued in 1979. Four studies examining the oncogenic potential of metolachlor have been submitted to the Agency. Two of these studies were in the Sprague-Dawley strain of rat and were found to be positive for the induction of neoplastic nodules in the liver at the highest tested dose level of 3000 ppm. The National Academy of Sciences (1980) has concluded that "the neoplastic nodule is a manifestation of the process of hepatocarcinogenesis...It is induced by a variety of hepatocarcinogens but not by noncarcinogenic agents." However, two mouse studies of metolachlor are considered to be negative with respect to oncogenic potential. The potential of metolachlor to cause cancer in laboratory animals, therefore, is substantially less clear than the weight of evidence on the carcinogenic potential of alachlor.

Based on the chronic rat study, the oncogenic potency of metolachlor (as indicated by the Q_1^* of 2.1×10^{-3}) appears to be much less than that of alachlor. However, it is noted that the testing of these two compounds was conducted by different laboratories and used different strains of rats. The use patterns, dietary Theoretical Maximum Residue Contributions, applicator exposure patterns and potential for drinking water contamination appear to be similar for the two compounds.

Table 26. Toxicity Data Base for Alternatives to Alachlor

	Pivotal Data	Data Gaps	Basis for Acceptable Daily Intake Calculation
Metolachlor	- 6 month dog feeding, NOEL = 100ppm - 2-Year supplementary (IBT) onco. in rat: weak oncogen i.e. liver tumors; - 2-Year chronic in rat (repeat study): weak oncogen - liver tumors, NOEL = 30 ppm (testicular atrophy) - 2-Year onco. in mouse negative at 3000 ppm (Highest Dose Tested (HDT)) Industrial Bio-Test, validated) - 3-generation rat reproduction = 300 ppm - Teratology rat NOEL = 360 mg/kg (HDT) - Teratology rabbit NOEL = 360 mg/kg - Mutagenicity: negative (2 tests) - Positive skin sensitizer - 2-Year onco. in mouse: negative at 3000 ppm (HDT)	Additional mutagenicity	6-month dog feeding, NOEL = 100 ppm weak oncogen: liver tumors, $O^*_1 = 2.1 \times 10^{-3}$
Vernolate	- 2-Year mouse feeding/onco. negative NOEL > 100 mg/kg/day (HDT)	All other pivotal data: chronic, onco., terato and reproduction	90-day rat feeding, not Core classified*: NOEL = 640 ppm
Pendimethalin	- Rabbit teratology, NOEL = 60 mg/kg (HDT) - 2-Year dog feeding, NOEL = 12.5 mg/kg/day (hepatic toxicity) - Mutagenicity: negative (2 tests)	All other pivotal data	90-day rat feeding, not Core classified: NOEL = 500 ppm
Metribuzin	- Rabbit teratology; NOEL = 15 mg/kg/ (HDT) - Mutagenicity: negative (3 tests) All the other Pivotal data were not Core classified: - 2-Year dog feeding, NOEL = 100 ppm - 2-Year rat feeding/onco., negative for oncogenicity; NOEL = 300 ppm - 2-Year mosue onco. negative at 3200 ppm (HDT) - 3-Gen. reproduction, NOEL = 300 ppm - Rat teratology, NOEL = 100 mg/kg (HDT)	Several pivotal studies were not Core classified and will be reevaluted in the Registration Standard.	Two-year dog feeding, not Core classified: NOEL = 100 ppm

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*The core classification system was developed by the Office of Pesticide Programs in 1977 to assess the adequacy of toxicology studies.

Table 26. Toxicity Data Base for Alternatives to Alachlor (Continued)

	Pivotal Data	Data Gaps	Basis for Acceptable Daily Intake Calculation
Oryzalin	- 3-Gen. reproduction NOEL = 250 ppm (LDT) - Rat teratology NOEL = 225 ppm (HDT) - Rabbit teratology NOEL = 125 mg/kg (HDT) - Chronic feeding/onco. in mouse NOEL = 500 ppm, not oncogenic at 3650 ppm (HDT) - 2-Year rat feeding/onco.: NOEL = 300 ppm, potential oncogen: skin tumors. - Mutagenicity: negative (3 studies)	One mutagenicity study: dominant lethal	90-day rat feeding not Core classified NOEL = 750 ppmgen in Potential oncogen in rat: skin tumors $Q_1^* = 3.375 \times 10^{-2}$
Trifluralin	- Rabbit teratology, NOEL = 450 mg/kg (Supplementary Data) - 4-Gen. rat reproduction, NOEL = 200 ppm (LDT) (Supplementary Data) All other pivotal data were not Core classified: - Mouse onco: positive, hepatocellular adenoma and carcinoma, alveolar-bronchiolar adenoma, and squamous-cell carcinoma in female mice. - Rat onco: negative at 6,500 ppm (HDT) - Reproduction - dog, NOEL = 25 mg/kg - 2-Year feeding rat, NOEL = 2,000 ppm - 3-Year dog, NOEL = 10 mg/kg (liver weight changes) - 2-Year dog, NOEL = 10 mg/kg (HDT)	Pending re-evaluation of pivotal data	90-day dog feeding, not Core classified: NOEL = 400 ppm

Table 26. Toxicity Data Base for Alternatives to Alachlor (Continued)

	Pivotal Data	Data Gaps	Basis for Acceptable Daily Intake Calculation
Propachlor	- Rat teratology, NOEL = 200 ppm (HDT) All the other pivotal data are not adequate to regulate this chemical: invalid or unvalidated IBT studies.	IBT replacement studies for all subchronic, chronic, and teratology data base.	90-day rat feeding, unvalidated IBT study with a NOEL = 266 ppm
Diphenamide	Pivotal data not Core classified: - 3 Gen. reproduction, NOEL = 10 mg/kg (fetotoxicity) - 2-Year rat feeding, NOEL = 10 mg/kg - 2-Year rat feeding, NOEL = 3 mg/kg	Pending reevaluation of pivotal data. Also no teratology study was initially submitted.	2-Year dog feeding, not Core classified: NOEL = 3 mg/kg
Atrazine	- Rat teratology, NOEL = 100 mg/kg - Negative mutagenicity (1 study) The other pivotal data are not adequate (Core supplementary) to regulate this chemical: - 2-Year dog feeding, NOEL = 150 ppm (LDT) - 3-Gen. rat reproduction, NOEL = 100 ppm (HDT) using the 80W formulation	Extensive data gaps: All chronic, teratology, reproduction and additional mutagenicity.	2-Year dog feeding, Core supplementary: NOEL = 150 ppm
Simazine	- 3-Gen. reproduction NOEL > 100 ppm (only one dose tested) - A questionable 2-year chronic feeding/onco. study in rat needs to be repeated, (NOEL > 100 ppm (HDT) using a 50% a.i. product)	Extensive data gaps: All chronic and teratology. A questionable onco. in rat needs to be replaced.	Apparently an Invalid study (unidentified at the present time) was used for ADI calculation.
Cyanazine	- teratology in Fisher rat: a potential weak teratogen, (NOEL for study not yet determined: 10 mg/kg for microophthalmia/anophthalmia, and pending additional studies, the NOEL may be lower than 1 mg/kg (LDT) for liver induced hernia) - teratology in SD rat: negative at 30 mg/kg (HDT), (however, MTD not tested). - teratology in rabbit: negative at 4 mg/kg (HDT), NOEL = 1 mg/kg/day - 2-year onco. in mice: negative at 1000 ppm (HDT)	All other pivotal data: chronic in 2 sp., onco. in rat, 3-gen. reproduction and additional mutagenicity studies	2-Year rat feeding, Core supplementary: NOEL = 12 ppm

F. Proposed Risk Reduction Measures

On June 19, 1984, Monsanto Chemical Co. submitted to the Agency risk reduction measures which the company proposed as conditions for the continued registration of alachlor. The Agency has examined each proposal. Presented below is the Agency determination of the impact of each risk reduction measure.

° Monsanto proposed to make a transition from the emulsifiable concentrate (EC) formulation to the microencapsulated (ME) formulation within the next five years. In the ME formulation alachlor is encapsulated in a polymer shell and suspended in a water formulation. The same amount of alachlor is applied per acre as with the EC, but Monsanto contends that the encapsulation process considerably reduces applicator exposure. The registrant estimates that applicator exposure to "free alachlor" will be reduced by more than 95% with the ME compared to the EC formulation. This would reduce applicator risk very substantially. However, no study has been received by the Agency which addresses the determination of "free alachlor" in the aqueous phase in the ME or any other formulation. The basis for the registrant's conclusion that potential exposure from the ME is only 2.6% of that for the EC is unclear. The Agency cannot assume that occupational exposure will be reduced to such an extent unless data are submitted to substantiate the claim.

° Monsanto proposed to eliminate all aerial application of alachlor products. The Agency supports the elimination of all aerial application uses of alachlor and that has been accomplished via the Registration Standard.

° Monsanto proposed elimination of the 6 and 8 lb/acre rates on soybeans. This alters one of the higher applicator exposure situations. The Agency accepted this proposal.

° Monsanto proposed to clarify and/or add protective clothing statements to alachlor labels. The Agency is imposing the addition of protective clothing statements for alachlor labels in the Registration Standard. The risk estimates in Table 23 which are predicated on the wearing of such protective clothing.

° Monsanto proposed to drop the use on potatoes from the alachlor labels. Potatoes represent the second highest contribution to the calculated Theoretical Maximum Residue Contribution (TMRC). Monsanto stated that withdrawing potatoes represents a 23.6% decrease in the TMRC which would result in a corresponding reduction in any dietary risk calculation. The results of this reduction are illustrated in Table 27.

° Monsanto proposed to develop methods and data to support a 10-fold reduction in meat, milk and egg tolerances. Current tolerances for these commodities are 0.02 ppm. If the tolerances for meat, milk and eggs were reduced to 0.002 ppm, a 35% reduction in the TMRC would result. Added to the withdrawal of potatoes, the registrant noted that this results in a 59% reduction in TMRC and a corresponding decrease in dietary risk calculations. Table 27 also shows the calculations resulting from the proposed lower tolerances. There is no change in the order of magnitude of the estimated risk. At the current time the Agency has no basis to assume that lower tolerances can be established for meat, milk and eggs. There is no adequate validated methodology available to measure residues below 0.02 ppm and that available methodology appears unable to measure certain metabolites which may represent significant portions of the residues of interest. Also, the metabolism of alachlor in animals is not understood. There are no valid feeding studies available reflecting maximum possible dietary intake of alachlor and its metabolites by animals. The analytical methodology and appropriate data are being required by the Registration Standard.

Table 27. Effect of Monsanto Proposals on Estimates of Dietary Risk

	Current Risk	Deletion of Potatoes	Deletion of Potatoes & Reduction of Milk, Meat, Egg Tolerances
TMRC (tolerance level)	6×10^{-4}	4×10^{-4}	2×10^{-4}
RISK	3×10^{-5}	3×10^{-5}	1×10^{-5}
% of ORIGINAL RISK ESTIMATE	100	76	42
Actual residue level	4×10^{-4}	3×10^{-4}	1×10^{-4}
RISK	3×10^{-5}	2×10^{-5}	7×10^{-6}
% of ORIGINAL RISK ESTIMATE	100	75	29

- Monsanto proposed grazing restrictions on peanuts or, alternatively, on everything but corn and sorghum. The restriction on feeding of peanut forage and hay would lower the average dietary burden of livestock, but the inadequacy of available metabolism, feeding and residue data does not allow the conclusion that the resulting residue level would be lower in meat, milk, poultry and eggs than 0.02 ppm. The data are being required by the alachlor Registration Standard. A recently submitted study indicates only 10% of soybean foliar and bean residues is converted to the 2,6-diethylaniline moiety which is measurable by available analytical methodology. The study demonstrates that 50% and 40%, respectively, of the total soybean foliar and bean ^{14}C residues contain alachlor metabolites convertible to 2-ethylaniline upon acid hydrolysis which will be detected by current methodology.

- Monsanto also suggested that the Agency consider the actual percentage of the crop that is treated in its estimate of dietary cancer risk. The Agency notes that the percentage of total acres treated with alachlor are 31, 28.5 and 38% for corn, soybeans and peanuts, respectively, based on a 1982 USDA survey. The percentage of acres of potatoes that is treated is much less (less than 2% of the total potato acreage). Since the use on potatoes is being cancelled, the Agency finds that the remaining risk is not substantially reduced by any attempt to adjust dietary risk for the percentage of corn, soybeans and peanut acres that are actually treated with alachlor. If the estimated exposures from directly consumed treated crops were reduced to reflect percentage of major crops treated, any such reduction could not be extrapolated to residues in animals and animal products because of the substantial gaps in our understanding of animal metabolism. The reduction in estimated average dietary risk would be about 10% for the general population assuming a uniform distribution of treated corn, soybeans and peanuts in individual diets and the reduction in risk will be even less for certain geographical areas where treated commodities are consumed at rates higher than the national average. In light of all the uncertainties inherent in the estimates of dietary exposure, the adjustment for percentage of major crop treated would not substantially improve the reliability of those estimates.

As evidenced by the above discussions, the risk reduction proposals suggested by Monsanto and adopted by the Agency are not sufficient to negate the need for a Special Review on alachlor.

III. Benefits Summary

A. Introduction

Alachlor is an herbicide produced in the U.S. by Monsanto Chemical Co. It has been estimated that in recent years approximately 90 to 95 million pounds of alachlor have been used annually as a pesticide active ingredient. Sites treated include preemergent application to corn, soybeans, peanuts, beans, potatoes, cotton, peas, sorghum, sunflowers, and ornamentals.

The information used to assess the benefits of alachlor was jointly derived from several sources - USDA, the States, Monsanto Chemical Company, Ciba-Geigy Corporation, and the EPA. The general approach of this analysis is to evaluate the economic impacts of an alachlor cancellation causing users to shift to alternative weed control agents. The alternatives to alachlor were chosen on the basis of cost, efficacy, and availability. Economic impacts on users, as well as for commodity markets and consumers are based on changes in production costs, crop yield reductions, and possible grower shifts to other agricultural enterprises. Impacts on users are considered on both a per-unit and aggregated basis at the regional and national level. Grower impacts are then utilized for projections at the commodity and consumer levels, where appropriate.

Analyses of the data available indicated the range of lost benefits of $40 million to $345 annually million depending on the alternatives adopted. Examination of the data and results indicate that the most likely first year loss in benefits would be about $157 million (Table 28). It is expected that impacts would remain near $157 million for 2 to 3 years following a cancellation of alachlor use. Economic impacts would then be expected to decline as existing weed control methods are adopted or new technologies become available. After 5 to 8 years, farmers and markets should be fully adjusted to the loss of alachlor. This represents losses due to both the increased cost of weed control and the decreased value of crop production. Cost estimates for continued use of alachlor are based on current costs and do not reflect any increases in the costs of using alachlor which might result from labeling changes such as classification for restricted use or requirements for protective clothing which were instituted with the issuance of the Registration Standard for alachlor. Those changes could affect the cost of alachlor use enough to remove the advantage in weed control costs which existed prior to the Registration Standard.

Monsanto Chemical Company advertising claims a 4 average bushel gain in corn yields for alachlor over metolachlor. If these estimates are accurate there would be losses to society of $330 to $430 million with consumer expenditures increasing by $670 to $800 million and farmers as a group experiencing gains of from $340 to $400 million. Although data were not available to indicate the distribution of the gains among alachlor users and non-users, indications are that those who do not use alachlor would experience the gains and users of alachlor would have a decrease in net returns. The impacts from the 4 average bushel gain in corn yields would represent a worst case projection of impacts of a loss of alachlor and do not take into account use of herbicides other than metolachlor as alternatives to alachlor on corn.

The magnitude of the impact of a loss of alachlor is highly dependent on the weed control programs which are used to replace alachlor. These programs would depend on the weed spectrums on those acres currently treated with alachlor and the portion of the acres with each weed spectrum. This information is not available. Therefore, the analysis of the loss of alachlor was based on the assumption that alternatives would replace alachlor at the same relative frequency as they are currently used.

The $10.5 million production loss for peanuts is the only such figure presented in Table 28. Determinations of production loss for other crops would be possible only if the entire product performance data base for alachlor vs. the alternatives were available; however, the wide range of available alternatives in most circumstances makes widespread production losses unlikely. There could be localized conditions where the use of alternatives would result in production losses to individual producers which could not be estimated with the information available.

If alachlor were unavailable for use on corn and soybeans, this analysis has assumed that in the first year after cancellation farmers would shift to the use of alternative herbicides. Since yield effects are expected only on peanuts and production costs have been higher with alternative controls, the earnings of some corn and soybean farmers would diminish. In the second and succeeding years, some corn and soybean farmers might respond to this lower income by shifting to the production of other profitable crops (mostly small grains or cotton).

It is estimated that about $20 to $25 million of the farm income loss would be shifted to consumers, an amount which is negligible in light of the total $21 billion domestic expenditure for corn and soybeans.

In calculating these impacts, it was assumed that only currently registered pest control methods would be available at the time of an alachlor cancellation. The estimated output loss to peanut growers is due to yield effects in south eastern states (Alabama, Florida, and Georgia) where weed control problems can not be alleviated with metolachlor, the most likely alternative (Schneider, 1984; Torla, 1984). Other herbicides not currently registered but showing promise for weed control in peanuts include : ethafluralin, vernolate, sethoxydim, acetochlor and fluazifop-butyl. It is not known if any of these chemicals will receive full registration or will serve as suitable alternatives.

In this preliminary assessment, EPA has not analyzed the economic impacts of the various potential changes in terms and conditions of continued registration which are identified as options in Chapter IV.

B. Field Corn

The loss of alachlor is estimated to increase cost of weed control of field corn by about $118 million assuming the cost of continued use of alachlor does not increase due to additional labeling requirements. The per acre weed control costs are estimated to range from a decrease of $7.37 per acre to an increase of $11.59 per acre. Variations in the production cost impacts are dependent on the particular weed problems and the cost of alternative controls (Torla, 1984).

There are limitations on the biological data base which could influence the estimates of the magnitude of the economic impacts of regulatory actions on alachlor. This analysis assumes that a shift to alternative weed controls would not result in any reduction in yields. Although data were not available to prove no yield losses would occur, available data indicated this to be a reasonable assumption. For most cases, this is a reasonable assumption since several alternatives are available to replace alachlor and a user should be able to identify a weed-control strategy without alachlor which would give comparable control. However, for no-till operations, which represent 3 percent of the affected acres, only metolachlor could replace alachlor and conditions such as regional weed infestations could exist for some producers where metolachlor would not be as effective and yield losses would result.

Certain limitations may affect the usefulness of alachlor alternatives. Examples of these limitations are soil texture, fertilizer compatability, need for soil incorporation and application technique. In no case do these limitations apply to every alternative to alachlor. Therefore, it is reasonable to conclude that at least one effective alternative exists for any situation (except for the certain no-till operations discussed above). In some situations, the limitations decrease the cropping options rather than prevent the use of alternative chemical controls. For example, in the case of crop rotation, there would be economic hardship in years when a first corn planting was lost due to cold, wet weather and a second corn planting without alachlor might be less profitable than planting to an alternative crop; and when the use of certain alternative chemicals may prevent the planting of an alternative crop due to phytotoxicity problems (Szuhay, 1984).

C. Peanuts

The cancellation of alachlor registrations for use on peanuts could result in losses to peanut producers of about $11.4 million annually. This estimate is based on likely decreases in the value of production of about $10.5 million and increases in the cost of weed control of about $0.9 million. Although the lost production is only about one percent of the U.S. peanut crop, it represents losses of about six percent to a portion of those producers using alachlor which could mean reductions in net returns of 40 to 60 percent for the producers in Alabama, Florida and Texas. The peanut crop is under a governmental allotment program and the USDA has been reducing the quantity of peanuts allowed to be produced because of surplus production. Therefore, the impact of any loss is expected to be borne directly by the producer and not shifted to the consumer (Torla, 1984).

The available biological data base for peanut production indicates that yield reductions could be expected for producers in certain geographical areas. In Oklahoma, copperleaf is a major weed pest in peanut fields. Metolachlor, the major alternative to alachlor on peanuts, does not control copperleaf. Control problems are also expected in Alabama, Florida and Texas. With the loss of alachlor, one additional cultivation would be necessary (in addition to metolachlor use) in all regions. Additional cultivations would require a fungicide spray at the time of cultivation to prevent white mold disease (Schneider, 1984). The estimated changed cost in weed control identified above takes into account the costs of increased cultivation and increased fungicide use in these areas.

D. Soybeans

The cancellation of alachlor use on soybeans is estimated to result in increased weed control costs of about $28 million. The per acre treatment cost impacts of an alachlor cancellation would range from a reduction of $2.26 to an increase of $9.55. Variations in the production cost impacts were dependent on the particular weed problems and the cost of alternative controls (Torla, 1984).

There were limitations on the biological data base which could influence the estimated magnitude of the economic impacts of a cancellation of alachlor. It was assumed that a shift to alternative weed controls would not result in any reduction in yields. For most situations, this is a reasonable assumption since alternatives will control most target weeds (Keitt, 1984).

E. Sweet Corn and Popcorn

It was estimated that a loss of alachlor use on popcorn and sweet corn would result in increased weed control costs of about $900,000. Since there is a very close similarity in growing conditions for field corn, popcorn and sweet corn, the reasons that losses are not expected for field corn also apply to these uses.

Sweet corn and popcorn are usually of higher unit value than field corn. The higher unit value could result in producers considering minor reductions in yield to be significant economic losses whereas comparable yield losses with field corn could be ignored (Torla, 1984).

F. Cotton, Dry Beans, Grain Sorghum, Green Peas, Lima Beans, Ornamentals, and Sunflowers

It is estimated that a cancellation of alachlor use would result in a $51,000 increase in the cost of producing cotton; a $3,000 to $4,000 production cost increase is expected for lima beans. The cancellation of alachlor use is expected to result in decreases in weed control costs of producing dry beans, grain sorghum, green peas, ornamentals, and sunflowers for those producers currently using alachlor. The magnitude of these impacts is expected to be small since alachlor is rarely used on these crops (Torla, 1984).

Alachlor is selected over other available alternatives for use on these minor crops, probably because of efficacy and/or crop injury reasons in localized production areas (Schneider, 1984).

G. Cabbage - Emergency Action

In a recent (1984) Agency approval of use under FIFRA Section 18, alachlor was determined to be the most efficacious weed control method available to cabbage growers in Illinois for control of Eastern black nightshade, galinoga and yellow nutsedge (Petrie, 1984).

Table 28. First Year Economic Impacts of Cancelling Alachlor

Use Site	Acres Planted (x 1000)	Acres Treated (x 1000)	Pounds a.i. Applied (x 1000)	Percent of Crop Treated	Percent of Alachlor Use on Crop	Change in Cost of Treatment	Decrease in Value of Production	User Impacts
Field corn	83,371	26,400	52,300	32	59	118.1	nominal	118.1[1]
Soybeans	70,003	18,300	30,900	26	35	28.2	nominal	28.2[1]
Peanuts	1,352	777	2,398	57	3	0.915	10.5	11.4
Potatoes	1,251	188-250	517-687	15-20	<1	0.100-0.132	not determined[2]	0.100 to 0.132
Sweet Corn/ Popcorn	812	203	406	25	<1	0.908	not determined[2]	0.908
Cotton	13,401	29-30	43-45	<1	<1	0.051	not determined[2]	0.051
Dry Beans	2,047	242-248	594	12	<1	-.230	not determined[2]	-.230
Grain sorghum	15,936	300-600	737-1,475	2-4	1-2	-1.01 to -2.02	not determined[2]	-1.01 to -2.02
Green peas (processing)	306	6-9	13-20	2-3	<1	-0.02 to -0.03	not determined[2]	-0.02 to -0/03
Lima beans (green)	65	6-9	13-20	9-14	<1	0.003-0.004	not determined[2]	0.003 to 0.004
Sunflowers	4,263	70	227	2	<1	0.326	not determined[2]	0.326
Ornamentals	n.a.	nominal	nominal	n.a.	n.a.	n.a.	not determined[2]	n.a.
TOTAL	192,807	46,521-46,896	88,148-89,072	-	-	146.3-147.4	-	156.8 to 157.9

Footnotes on next page.

1/ About $20 to $25 million of corn and soybean impact could be shifted to the consumer.

2/ Decrease in value of production was not determined for these crops due to the unavailability of comparative product performance data for alachlor vs. alternatives.

IV. Additional Grounds for Review

As discussed in detail in Chapter II of this document, data have shown that alachlor is oncogenic in test animals. The data and analyses available at this time with respect to dietary exposure are not sufficient to warrant the issuance of a final regulatory decision. The Agency specifically solicits further evidence bearing on these possible adverse effects. All comments and information received with respect to the potential adverse effects, including analysis, may serve as a basis for a final decision on the registration of pesticides containing alachlor.

A. Risk/Benefit Information

The Agency's principal concern is that significant continued long-term or lifetime exposure to alachlor may pose a risk to human health. Several long-term feeding studies in laboratory animals indicate that alachlor causes tumors at a number of sites in the body and, therefore, human exposure to alachlor raises public health concerns. There are three sources of possible human exposure to alachlor.

First, approximately 90 million pounds of alachlor are used annually to treat about 45 million acres of cropland. As many as one million persons are involved in handling and applying alachlor. Most, if not all, are exposed at levels which raise concerns about human health if exposures were to continue over their working lifetime.

Second, in an area heavily used for growing the principal crops on which alachlor is applied, residues in surface water and ground water used as municipal drinking water supplies are found to persist at levels which raise concerns about health risks to persons who might be exposed over long periods.

The third source of possible exposure to alachlor is through consumption of treated crops containing residues of the chemical. Information on the extent to which alachlor residues exist in individual food commodities is very limited. Residues may be found in treated crops. If all treated commodities and animal products from animals consuming treated feed were found to contain alachlor and its important metabolites at or near tolerance levels, the resulting exposure to humans over time would raise serious health concerns.

Estimates of human health risk to alachlor are presented in Chapter II of this document. Registrants and other interested persons are invited to examine the basis for the Agency's decision to initiate the Special Review and may submit data and information. Registrants and users may also suggest methods to reduce risk of use of the pesticide to acceptable levels.

The regulatory options which will be considered by the Agency in reaching a final regulatory decision are: (1) continuation of registration without further changes in the terms and conditions, (2) continuation of registration with modification to the terms and conditions of registration, and (3) cancellation of registration. Some suggested risk reduction measures short of cancellation on which the Agency would like to receive comments and information are:

1. Requiring alachlor to be marketed only in closed systems.

Handling systems utilizing transfer probes or pumps would avoid direct handling of the container and would reduce applicator exposure to the product. Monsanto has committed to increase the use of bulk and 55 gallon reduced exposure systems to 55% of the total alachlor sales in 1985 and to 65% by 1937. The Agency will be examining the feasibility of requiring that all alachlor be sold in reduced exposure systems.

2. Requiring alachlor to be soil-incorporated.

At the present time only about 25% of the alachlor applied is incorporated. The Agency is examining the extent to which runoff and associated surface water contamination can be eliminated if alachlor is no longer surface-applied. In conjunction with this, the Agency will also consider the results of leaching/mobility studies required by the alachlor Registration Standard. That is, while incorporation of alachlor may reduce runoff to surface water, it may cause alachlor to leach into ground water.

3. Restricting alachlor use only to certified applicators.

Restricting the use of alachlor to certified applicators should help reduce the chance for accidental or careless excess occupational exposure to alachlor.

4. Limiting application rate of alachlor to 2 lb/acre.

Monsanto contends that the 4 lb/acre rate is necessary for acceptable weed control under conditions of high infestation of difficult to control weeds, and where soil texture and organic matter content reduce herbicidal activity. The 4 lb rate is used on only 5.2% of the total alachlor treated acres. The Agency will be considering limiting alachlor application to 2 lb/acre to further reduce worker exposure. Implications of this restriction to be considered are a reduction in the effectiveness of weed control in certain geographical areas or a reduction in the number of uses for alachlor.

5. Allowing marketing of only the ME formulation.

Monsanto contends that the ME formulation considerably reduces applicator exposure to the active ingredient. If this is true, it may mitigate some of the Agency's concerns. However, at the present time Monsanto has not submitted the appropriate data to substantiate the claim.

In order to carry out the benefit analysis of the consequences of limiting or cancelling uses of alachlor, EPA also solicits comments from registrants, users or other interested parties in regard to the following aspects, for each crop for which alachlor is registered. The experience of farmers that use alachlor, particularly when documented by records, as well as results of surveys and comparative experiments, is desired. Of special interest are (1) data from carefully designed and executed field scale yield comparisons which compare alachlor with potential alternative herbicides, (2) data which relate yield differences to one or more specific conditions (of major importance are soil types, moisture and temperature in relation to time of planting and application of herbicides, weed pressure, crop variety, geographic location, and method and timing of herbicide application), and (3) information on relative crop tolerance to herbicides and tank mix combinations, especially in relation to environmental factors, e.g. cold, wet weather shortly after planting.

Also important is information on:

1. Weed control programs involving alachlor on all registered sites. Important aspects are:

   a. the crop involved (especially those other than corn, soybeans and peanuts),

   b. number of acres treated in the program,

   c. regions where the program is used,

   d. other chemical, rotational and mechanical components (e.g. cultivation) of the program,

   e. rate, timing, and frequency of application of herbicides or of mechanical treatments.

2. Alternative weed control practices that would be used if alachlor uses were limited or cancelled. In addition to the information supplied under Item 1 above, include:

   a. changes in the use of chemical or mechanical weed controls,

   b. other changes in farming practices resulting from the use of the alternative weed control,

c. advantages and disadvantages resulting from the change of programs.

3. The impact of limiting or cancelling alachlor use upon double-cropping, no-till and minimum-till farming, and other practices designed to conserve soil, energy, and/or time. Include estimates of the affected acreage and indicate the region(s) where the impact will occur.

4. The current availability of alternative chemicals or mechanical equipment, and any expected changes in their prices if alachlor were to be limited or cancelled.

5. The impacts on commodity export markets if alachlor use were limited or cancelled.

6. The impact on the cost of agricultural subsidy programs administered by USDA, if alachlor use were limited or cancelled.

B. Rebuttal Submission Procedures

The registrant and other interested parties will have 45 days from the date this document is received or until 45 days after the date of publication of the notice in the FEDERAL REGISTER (whichever is later) to submit evidence in rebuttal to the Agency's presumption.

C. Duty to Submit Information on Adverse Effects

Registrants are required by Section 6(a)(2) of FIFRA to submit any additionl information regarding unreasonable adverse effects on man or the environment which comes to their attention at any time. The registrant of alachlor products must immediately submit any published or unpublished information, studies, reports, analyses, or reanalyses regarding any adverse effects associated with alachlor in animal species or humans, and claimed or verified accidents to humans, domestic animals or wildlife which have not been previously submitted to EPA. These data should be submitted with a cover letter specifically identifying the information as being submitted under Section 6(a)(2) of FIFRA. In light of this Special Review and the requirements of FIFRA 6(a)(2), the registrant should notify EPA of any studies on alachlor currently in progress, their purpose, the protocol, the approximate completion date, a summary of all results observed to date, the name and address of the laboratory performing the studies, and a statement as to whether these studies are being conducted in accordance with the Good Laboratory Practices specified in 48 FR 53946.

D. Public Comment Opportunity

During the time allowed for submission of rebuttal evidence, specific comments are solicited on the presumptions and analyses set forth in this Position Document, the FEDERAL REGISTER notice and in the Guidance Document. In particular, any documented episodes of adverse effects on humans or domestic animals should be submitted to the Agency as soon as possible. Any information as to any laboratory studies in progress or completed should be submitted to the Agency as soon as possible with a statement as to whether those studies are in compliance with the Good Laboratory Practices specified in 48 FR 53946. Specifically, information on any adverse toxicological effects of alachlor, its impurities, metabolites and degradation products is solicited. Similarly, submission of any studies or comments on the benefits from the use of alachlor is requested. All comments and information and analyses which come to the attention of EPA, may serve as a basis for final determination of regulatory action following the Special Review.

Information submitted in any comment concerning this document may be claimed confidential by marking any part or all of that information as "Confidential Business Information" (CBI). Information so marked will not be disclosed except in accordance with procedures set forth in 40 CFR Part 2. A copy of the comment containing material claimed to be CBI must be submitted with the CBI portions deleted for inclusion in the public record. Information not marked confidential may be disclosed publicly by EPA without prior notice to the submitter.

During the comment period, interested members of the public or registrants may request a meeting to discuss the risk issues and methods of reducing risks. Prior to such meeting, the Agency will place an agenda and list of meeting participants in the public docket. Any member of the public interested in obtaining a copy of the agenda prior to the meeting with the Agency to discuss issues in connection with this Special Review should notify the contact person listed in the FEDERAL REGISTER notice. Any records pertaining to such meetings, including minutes, agendas and comments received will be filed in Room 236, CM #2, 1921 Jefferson Davis Highway, Arlington, VA. 22202.

REFERENCES

Ahmed, F.E., A.S. Tegeris, P.C. Underwood, et al (1981) Alachlor: Six-Month Study in the Dog: Testing Facility's Report No. 7952; Sponsor's Report No. PR-80-015. (Unpublished study including submitter summary, received Dec. 1, 1981 under EPA Reg. No. 524-316; prepared by Pharmacopathics Research Labs., Inc., submitted by Monsanto Co., Washington, D.C., CDL: 246229-A and 246293.

Atkins, E.L., E.A. Greywood and R.L. Macdonald (1973) Toxicity of Pesticides and Other Agricultural Chemicals to Honey Bees: Laboratory Studies. Rev. by Univ. of California, Riverside, CA., Dept. of Entomology, Agricultural Extension Service. (Also in unpublished submission received April 2, 1980 under EPA Reg. No. 464-556, submitted by Dow Chemical U.S.A., Midland, MI, CDL: 242149-z).

Baker, B. David, et al (1981) The concentrations and transport of pesticides in Northwestern Ohio Rivers. Water Quality Laboratory, Heidelberg College, Tiffin, Ohio.

Baker, B. David. (1982) Pesticide Monitoring Notes 1982. Water Quality Laboratory, Heidelberg College, Tiffin, Ohio, Dec. 10, 1982.

Baker, B. David. (1983a) Studies of sediment, nutrient and pesticide loading in selected Lake Erie and Lake Ontario tributaries. "Part IV Pesticide concentrations and loading in selected Lake Erie tributaries, 1982," July 1, 1983. Water Quality Laboratory, Heidelberg College, Tiffin, Ohio.

Baker, B. David. (1983b) Herbicide contamination in municipal water supplies of Northwestern Ohio. Draft final report by Heidelberg College, Tiffin, Ohio, under assistance agreement #R00572701 from U.S.EPA, Oct. 2, 1983.

Baker, B. David. (1984a) A table summarizing our rainwater analyses for herbicides in a letter to John McManus of Am. Electric Power Service Corp. from David Baker, Aug. 16, 1984. Heidelberg College; Tiffin, Ohio.

Baker, B. David. (1984b) Preliminary printout of 1984 data for pesticide measurements. Personal communication to P.R. Datta, Sept. 10, 1984. Heidelberg College, Tiffin, Ohio.

Binder, M. Daniel. (1984) Annual Report on water quality treatment and monitoring, 1981, 1982, 1983 for City of Columbus, Ohio. Personal communication to P.R. Datta, Sept. 12, 1984.

Carsel, R.F., L.A. Mulkey, M.N. Lorber, and L.B. Baskin. (1984) In press. The Pesticide Root Zone Model (PRZM): A Procedure for Evaluating Pesticide Leaching Threats to Ground Water. U.S. Environmental Protection Agency.

Ciba-Geigy Corp. (1979) Two-year Chronic/Oncogenicity Oral Toxicity Study in Albino Rats. Study No. 622-07926. Unpublished study dated Feb. 9, 1979, performed by IBT, Decatur, Ill., submitted by Ciba-Geigy Corp. CDL: 244166.

Cohen, S.Z., S.M. Creeger, R.F. Carsel and C.G. Enfield (1984) Potential for Pesticide Contamination of Ground Water Resulting From Agricultural Uses in Treatment and Disposal of Pesticides. American Chemical Society Symposium Series #259.

Coleman, D.L. and W.R. Gaffey (1980) A Study of Individuals Exposed to Alachlor: Ocular Examinations for Uveitis. Unpublished study received July 30, 1980 under EPA Reg. No. 524-285; submitted by Monsanto Chemical Co., Washington, D.C.; CDL: 242943-A.

Daly, I.W., G.K. Hagan,R. Plutnick, et al (1981a) An Eighteen-Month Chronic Feeding Study of Alachlor in Mice: Project No. 77-1064. Final report. Unpublished study received July 1, 1981 under EPA Reg. No. 524-285, prepared by Bio/dynamics, Inc., submitted by Monsanto Co., Washington, D.C., CDL: 070168-A, 070169.

Daly, I.W., J.B. McCandless, H. Jonassen, et al (1981b) A Chronic Feeding Study of Alachlor in Rats, Project No. 77-2065. Final Report. Unpublished study received Jan. 5, 1982 under EPA Reg. No. 524-285, prepared by Bio/dynamics, Inc., submitted by Monsanto Co., Washington, D.C., CDL: 070586-A, 070587, 8, 9 & 90.

Danhaus, R.G., J.L. Stragy and S. Dubelman (1980) Residues of Alachlor and Atrazine in Field Treated Corn Following Preemergent and Lay-by Applications of Lasso™ or Lasso™ and Atrazine Tank Mixes; Report No. MSL-1105. Unpublished study received April 24, 1980 under EPA Reg. No. 524-285; prepared in cooperation with ABC Labs, Inc., submitted by Monsanto Co., Washington, D.C., CDL: 099396.

Dean, J.D., P.P. Jowise, and A.S. Donigian, Jr. (1984) Leaching Evaluation of Agricultural Chemicals (LEACH) Handbook (EPA-600/3-84-068). U.S. Environmental Protection Agency. U.S. EPA contract #68-03-3116.

Dodd, Nancy (1984a) Memo to Robert J. Taylor and Toxicology Branch dated June 29, 1984. Feeding of radiolabeled alachlor metabolites to laying hens, Accession number 252792. Submitted in connection with EPA Reg. No. 524-316.

Dodd, Nancy (1984b) Memo to Robert J. Taylor and Toxicology Branch dated July 3, 1984. Feeding of radiolabeled alachlor metabolites to lactating goats, Accession number 252793. Submitted in connection with EPA Reg. No. 524-316.

Environmental Protection Agency (1977) "Drinking Water and Health", a report from National Research Council and the U.S. EPA.

Environmental Protection Agency (1982) STORET Users Handbook. The Right Answers for STORET Users. Third Edition. February, 1982.

Environmental Protection Agency (1984) Guidelines for Risk Assessment of Suspected Carcinogens, EPA, Office of Research and Development, October, 1984 draft.

Farrow, Michael G. (1984) *In Vivo* Bone Marrow Chromosome Study in Rats with Alachlor. Unpublished study dated March 1, 1984, submitted under EPA Reg. Nos. 524-285, 296, 314 and 316, prepared by Hazelton Labs., Inc., Vienna, Va. 22180, submitted by Monsanto Chemical Co., Washington, D.C., CDL: 253308.

Fink, R., et al (1979) Final Report: Acute Oral LD_{50} - Bobwhite Quail: Project No. 139-179. Unpublished study recieved June 1, 1981 under EPA Reg. No. 524-285, prepared by Wildlife International Ltd., submitted by Monsanto Co., Washington, D.C., CDL: 245260-A.

Forbis, A.D., and W.A. McAllister (1978) Acute Toxicity of Technical Alachlor to Rainbow Trout (*Salmo gairdineri*). Unpublished study received August 16, 1978 under EPA Reg. No. 524-385, prepared by Analytical Biochemistry Laboratories, Inc. submitted by Monsanto Co.

Frank, R. (1984) Communication prepared by Richard Frank, Ontario Ministry of Agriculture and Food, University of Guelph, July 27, 1984.

Hallberg, G.R., B.E. Hoyer, E.A. Bettis, and R.D. Libra. (1983) Hydrogeology, Water Quality, and Land Management in the Big Spring Basin, Clayton County, Iowa. A report by the Iowa Geological Survey on contract number 82-5500-02 from the Iowa Department of Environmental Quality.

Hawf, L., D. McCall and L. Gingerich (1983) Teleconference with B.A. Schneider, EPA, OPP, BUD, SSB with Monsanto Agricultural Products, Inc., March 15, 1983.

IARC (1980) IARC Monographs on the Evaluation of Carcinogenic Risks of Chemicals to Humans, "Some Pharmaceutical Drugs." Volume 24. International Agency for Research in Cancer, Lyon, France. September, 1980.

Johanson, R.C., J.C. Imhoff and H.H. Davis, Jr.(1980) Users Manual for Hydrological Simulation Program - Fortran (HSPF). Grant No. R804971-01 for U.S. Environmental Protection Agency. EPA-600/9-80-015.

Johnson, H.P. and J.L. Baker (1982) Field-to-stream transport of agricultural chemicals and sediment in an Iowa Watershed: Part I: Data base for model testing (1976-1978).

Johnson, H.P. and J.L. Baker (1984) Field-to-stream transport of agricultural chemicals and sediment in an Iowa Watershed: Part II: Data base for model testing (1979-1980).

Keitt, G.W., Jr. (1984) Biological Data Base for Exposure Analysis and Preliminary Benefits Analysis of Alachlor on Soybeans and Ornamentals. Science Support Branch, BUD/OPP/OPTS/EPA.

Konishi, Yoichi, A. Kawabata, A. Denda, T. Ikeda, H. Katada, H. Maruyama and R. Higashiguchi (1980) Forestomach Tumors Induced by Orally Administered Epichlorohydrin in Male Wistar Rats. Gann, 71, 922-2. December, 1980.

Kovacs, Martin F., Jr. (1984) Memo to Robert J. Taylor and Toxicology Branch dated April 23, 1984. PP#0F2348 Alachlor (Lasso™) in or on corn forage and fodder and PP#3F2832 Alachlor on soybean hay. Comments on additional corn and soybean metabolism studies dated September 16, 1983 (Accession number 251375).

Laskin, Sidney, A.R. Sellakumer, M. Kuschner, N. Nelson, S. LaMendula, G.M. Rusch, G.V. Katz, N.C. Dulak and R.D. Albert (1980) Inhalation Carcinogenicity of Epichlorohydrin in Noninbred Sprague-Dawley Rats. Journal of the National Cancer Institute 65 (4): 751-7. October 1980.

Lauer, R., D.D. Arras, J.L. Stranz, et al (1979) Residues of Alachlor and Atrazine in Field Tested Sorghum Following Pre- or Postemergent Applications with Lasso™ or a Lasso™ and Atrazine Tank Mix: Report No. MSL-1033. Unpublished study received March 25, 1980 under EPA Reg. No. 524-285, prepared in cooperation with ABC Labs., Inc., submitted by Monsanto Chemical Co., Washington, D.C.; CDL: 099326.

Lauer, R. and D.D. Arras (1981) Aerial and Ground Applicator Exposure Studies with Lasso™ Herbicide Under Actual Field Conditions. Report No.: MSL-1889. Submitted by Monsanto Co. CDL: 070591.

Lavy, T.L. (1974) Mobility and deactivation of herbicides in soil-water systems: Project A-024-NEB. Available from NTIS, Springfield, VA: PB-238-632; unpublished study received July 19, 1978 under EPA Reg. No. 201-403; prepared by Univ. of Nebraska, Water Resources Research Institute, submitted by Shell Chemical Co., Washington, D.C., CDL: 234472-P.

Libra, R.D., G.R. Hallberg, G.G. Ressmeyer, and B.E. Hoyer. (1984) I. Groundwater Quality and Hydrogeology of Devonian-Carbonate Aquifers in Floyd and Mitchell Counties, Iowa. A report by the Iowa Geological Survey on grant number G0072737-01 from U.S. EPA.

Maryland Department of Health and Mental Hygiene (1983) Results of a Maryland Ground Water Herbicide Survey. A report on a survey by the Office of Environmental Programs, Maryland DHMH, Fall 1983.

Miltner, D. (1984) Personal communication to P.R. Data from D. Miltner, EPA Drinking Water Laboratory, Cincinnati, Ohio, Sept. 14, 1984.

Mirsalis, J.C. (1984) An Evaluation of the Potential of Alachlor to Induce Unscheduled DNA Synthesis in the *In Vivo-In Vitro* Hepatocyte DNA Repair Assay. Unpublished study dated March 5, 1984, submitted under EPA Reg. Nos. 524-285, 296, 314 and 316, prepared by SRI International, Menlo Park, CA 84025, submitted by Monsanto Chemical Co., Washington, D.C., CDL: 253308.

Monsanto Co. (1967) Metabolism Section - soybeans and corn, Section D-II of PP # 7F0622. Lasso™. Unpublished study received under EPA Reg. No. 524-?. CDL: 115143.

Monsanto Co. (1969) Metabolism Section - Peanuts and cotton. Section D-II of PP # 9F0776. Lasso™. Unpublished study received under EPA Reg. No. 524-?. CDL: 115827.

Monsanto Co. (1973) Section A of Pesticide Petition No. 3F1406, submitted by Monsanto Co. RCB Accession No. 118284.

Monsanto Co. (1978a) Acute Oral-Rat, Acute Dermal-Rabbit. Submitted by Bio-Dynamics, Inc., PD-77-433 on June 28, 1978 Unpublished study received 1978; CDL: 241273.

Monsanto Co. (1978b) Primary Eye and Primary Dermal Irritation-Rabbit. Submitted by Bio-Dynamics, Inc., PD-77-433 on March 22, 1978. Unpublished study received 1978; CDL: 241273.

Monsanto Co. (1979a) Environmental Chemistry of Alachlor. Unpublished study received Oct. 17, 1979 under EPA Reg. No. 524-285, 296 and 314, prepared by Monsanto Agricultural Products Co., submitted by Monsanto Co., Washington, D.C.; CDL: 241135 & 241136.

Monsanto Co. (1979b) Section A of Pesticide Petition No. 9F2144, submitted by Monsanto Co. RCB Accession No. 225417.

Monsanto Co. (1981a) Elimination of ^{14}C-alachlor in Monkeys. Study No. MA-81-261, prepared by the Univ. of California School of Medicine. Submitted by Monsanto Co., Washington, D.C., on November 28, 1981. CDL: 070592, 247937.

Monsanto Co. (1981b) *In vitro* dermal penetration of ^{14}C-alachlor in human skin. Study No. UW-81-262, prepared by the Univ. of Washington School of Medicine, Washington. Submitted by Monsanto Co., Washington, D.C. on November 20, 1981. CDL: 070592.

Monsanto Co. (1981c) Acute Inhalation LD_{50}-Rat. Submitted by Bio/Dynamics, Inc., PD-81-183 on Dec. 3, 1981. Unpublished study received 1981; CDL: 248053.

Monsanto Co. (1982) Environmental Fate of Microencapsulated Alachlor: Vol I & II. Unpublished study received May 26, 1982 under EPA Reg. No. 524-344, prepared by Monsanto Agricultural Products Co., submitted by Monsanto Co., Washington, D.C., CDL: 070841.

Monsanto Co. (1983a) Rat Metabolism Study. MSL-3198, R.D. 493. Part I and II. Unpublished study received Oct. 1983 under EPA Reg. No. 524-316; prepared by Monsanto Agricultural Products Co., submitted by Monsanto Co., Washington, D.C.; CDL: 251543 and 251544.

Monsanto Co. (1983b) Additional Corn and Soybean Metabolism Studies to Support the Registration of Lasso®, EC, II and ME. RD No. 489, Special Report MSL-3132. Unpublished study received Sept. 16, 1983 under EPA Reg. Nos. 524-285, 296, 314 and 344; prepared by Monsanto Agricultural Products Co., submitted by Monsanto Co., Washington, D.C.; CDL: 251375.

Monsanto Co. (1984a) Dermal Sensitization-Guinea Pig. Submitted on March 24, 1984. Unpublished study received 1984; CDL: 252772.

Monsanto Co. (1984b) Metabolism of Synthetic ^{14}C-Labeled Plant Metabolites of Alachlor in Laying Hens, Part I: Distribution of ^{14}C-Metabolites in Eggs, Tissues and Excretia. RD No. 532. Unpublished study received in 1984 under EPA Reg. No. 524-314; CDL: 252792.

Monsanto Co. (1984c) Metabolism of Synthetic ^{14}C-Labeled Plant Metabolites of Alachlor in Lactating Goats, Part I: Distribution of ^{14}C Metabolites in Milk, Tissues and Excretia. RD No. 531. Unpublished study received in 1984 under EPA Reg. No. 524-314; CDL: 252793.

Mulkey, L.A. and A.S. Donigan (1984) Modeling Alachlor Behavior in Three Agricultural River Basins. U.S. Environmental Protection Agency.

NAP (1983) Risk Assessment in the Government: Managing the Process. National Academy Press, Washington, D.C.

National Academy of Sciences (1980) "Histologic Typing of Liver Tumors of the Rat." Journal of the National Cancer Institute, Vol. 64, No. 1, 1980, p.185.

National Research Council (1977) Drinking Water and Health, Report from National Research Council and U.S. EPA.

OSTP (1984) Chemical Carcinogens, Notice of Review of Science and its Associated Principles. Office of Science and Technology Policy. Federal Register Vol. 9, Tues. May 22, 1984. pp. 21594-21661.

Petrie, Richard C. and B.A. Schneider (1984) Preliminary Biological Analysis of Alachlor (090501) Use on Potatoes, Sunflowers and Grain Sorghum. June, 1984. OPP/BUD/SSB.

Rodwell, D.E., and E.J. Tacher (1980) Teratology Study in Rats: IRDC No. 401-058; IR-79-020. Unpublished study including submitter summary, received Oct. 16, 1980 under EPA Reg. No. 524-385; prepared by International Research and Development Corp., submitted by Monsanto Co., Washington, D.C.; CDL: 243506-A.

Schardein, James L. (1984) Teratology Study in Rabbits with Alachlor (IR-83-045). Unpublished study received in 1984 under EPA Reg. No. 524-316, prepared by International Research and Development Corp., submitted by Monsanto Agricultural Products Co., St. Louis, MO; CDL: 252570.

Schmitt, R.D. (1977) Food Factors. Memorandum: to O.E. Paynter. September 4, 1977. Environmental Protection Agency.

Schneider, B.A. and R.C. Petrie (1984) Biological Data Base (Track B) for Preliminary Benefits Analysis of Alachlor (090501) Use on Peanuts, Dry Beans (All Types) Including Lima Beans (Green), Red Kidney Beans and Mung Beans, Green Peas, Cotton. May, 1984. EPA/OPP/BUD/SSB.

Schroeder, R.D., G.K. Hogan, M.E. Smock, et al (1981) A Three-Generation Reproduction Study in Rats with Alachlor: Project No. 77-2066. Final Rept. Unpublished study received July 10, 1981 under EPA Reg. No. 524-285; prepared by Bio/Dynamics, Inc., submitted by Monsanto Co., Washington, D.C.; CDL: 070177-A.

Shirasu, et al (1980) Microbial Mutagenicity Study, received Feb. 1980 under EPA Reg. No. 524-316. Prepared by Institute of Environmental Toxicology; Kodaira, Japan; submitted by Monsanto Co., Washington, D.C.; CDL: 248053.

Spalding, R.F., G.A. Junk, and J.J. Richard (1980) Pesticides in Ground Water Beneath Farmland in Nebraska, August, 1978. Pesticide Monitoring Journal 14(2): 70-73.

Stout, L.D., et al (1983a) A Chronic Study of Alachlor Administered in Feed to Long-Evans Rats. EHL #800218, Project #ML-80-186, Report MSL-3282/3284. Vol. I & II. Unpublished study received Feb. 28, 1984 under EPA Reg. No. 524-316, prepared by Monsanto Environmental Health Laboratory(EHL) submitted by Monsanto Co., Washington, D.C., CDL: 252496-7.

Stout, L.D., et al (1983b) A Chronic Study of Alachlor Administered in Feed to Long-Evans Rats. EHL #800218, Project #ML-80-186, Report MSL-3282/3284. Vol. III of III. Unpublished study received Feb. 28, 1984 under EPA Reg. No. 524-316, prepared by Monsanto Environmental Health Laboratory (EHL), submitted by Monsanto Co., Washington, D.C., CDL: 252498.

Sutherland, M.L., T.G. Curtis, W.A. Darlington, and J.T. Marvel (1972) Final report on Lasso and the environment: Part 4: Photolysis of Lasso on soil and in water: Agric. Research Report No. 262. Unpublished study received June 29, 1978 under PP # 3F1372; submitted by Monsanto Co., Washington, D.C., CDL: 093660-L.

Szuhay, D.W. and G.W. Keitt, Jr. (1984) Biological Data Base for Exposure Analysis and Preliminary Benefits Analysis of Alachlor on Corn. Science Support Branch, BUD/OPP/OPTS/EPA.

Thompson, C.M., A.D. Forbis, and W.A. McAllister (1978) Acute Toxicity of Technical Alachlor (AB-78-166) to Bluegill Sunfish (Lepomis macrochirus). Unpublished study received August 16, 1978 under EPA Reg. No. 524-283; prepared by Analytical Biochemistry Laboratories, Inc., submitted by Monsanto Co., Washington, D.C., CDL: 234628-C.

Torla, R. (1984) Preliminary Benefit Analysis of Alachlor. Economic Analysis Branch, Benefits and Use Division, Office of Pesticide Programs, Preliminary Draft, May 1984.

U.S. Environmental Protection Agency (1984) Federal Reporting Data System. Facilities and Population Served by Drinking Water Supply Source; Community Active Systems, Not Including Indian Lands, FY 1983 (FRDS07, April 21, 1984).

Wehtje, G. et al (1981) Atrazine contamination of ground water in the Platte Valley of Nebraska from nonpoint sources. The Science of the Total Environment. 21, 47-51, 1981.

Weidner, C.W. (1974) Degradation in ground water and mobility of herbicides. Master's thesis, Univ. of Nebraska, Dept. of Agronomy. Unpublished study received July 19, 1978 under EPA Reg. No. 201-403, submitted by Shell Chemical Co., Washington, D.C., CDL: 234472-O.

Wilson, G.R., et al (1981) Residues of Alachlor in Sorghum Forage, Stover and Grain. Report No. MSL-1577. Unpublished study received May 27, 1981 under EPA Reg. No. 524-285; prepared by ABC Labs., Inc., submitted by Monsanto Chemical Co., Washington, D.C.; CDL: 245225.

Yu, C.C., G.M. Booth and D.J. Hansen (1971) Fate of alachlor and propachlor in a model ecosystem. Unpublished study received June 29, 1973 under PP # 3F1372; prepared in cooperation with Illinois Natural History Survey and others, submitted by Monsanto Co., Washington, D.C., CDL: 093660-Q.

Zager, Edward and Michelle L. Loftus (1984) Memo to Diane Ierley dated August 22, 1984. Residue Chemistry Branch response to the comments of the Assistant Administrator's staff on the alachlor Position Document.

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